

Lecture Series “Clinical Cases”

Hematology & Oncology

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Abt. für Hämatologie, Onkologie und Immunologie

Term definition: Hematology

Hematology: Study of the diseases of the blood, bone-marrow and the lymphatic system.

- **Benign Hematology**
 1. Thrombophilia, Hemophilia (Hemostaseology)
 2. Immune Thrombocytopenias
 3. Anemias

- **Malignant Hematology**
 1. Non Hodgkin's Lymphoma
 2. Hodgkin's Disease
 3. Leukemias

Term definition: Oncology

Oncology: Study of malignant diseases.

- Brain Tumors
- Bone and Soft Tissue Tumors
- Lung Tumors
- Gastrointestinal Tumors
- Genitourinary Cancer
- Breast Cancer
- Skin Cancer
- Hematologic Malignancies (Leukemia, Lymphoma)

Term Definition: Therapy Goals

Curative Therapy: The cure of the patient is the goal of the therapy.

Palliative Therapie: The cure of the patient is not possible due to advanced disease. The goal is to prolong life and to ameliorate symptoms.

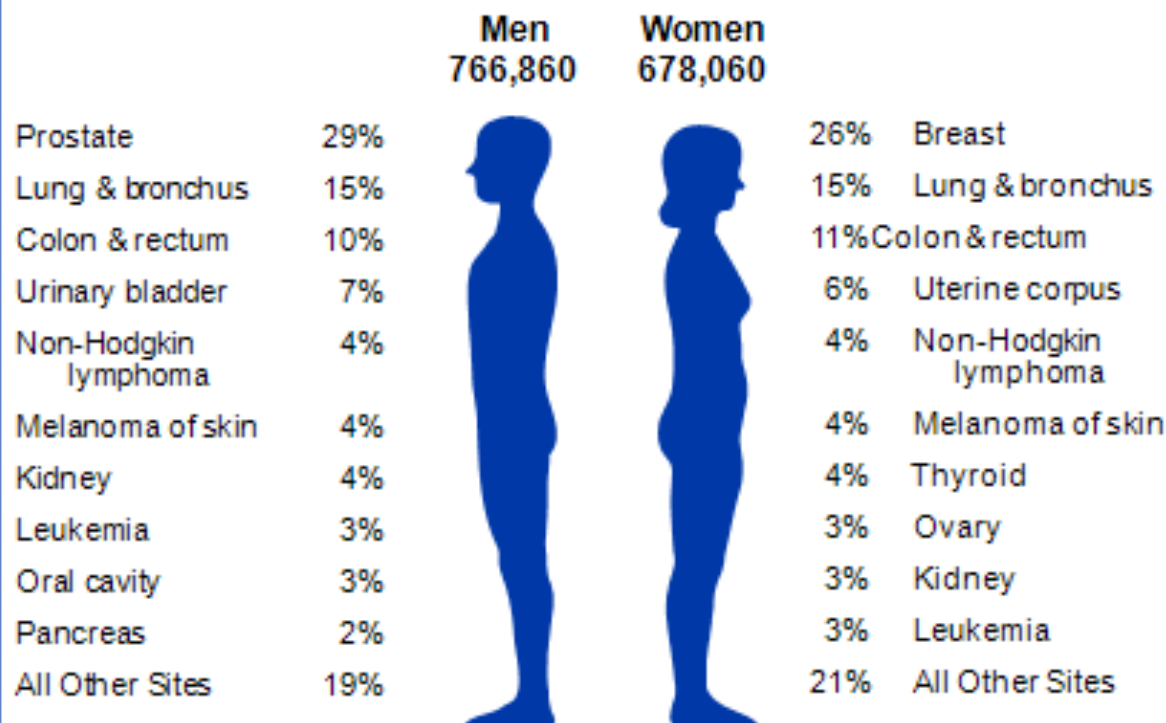
Best Supportive Care: No cancer-specific therapy. Main goal is the amelioration of disease symptoms like pain etc.

Is Oncology important ?

- Every 2nd person will develop cancer.
- Every 4th person will die of cancer.
- Cancer is a disease of advanced age.
- The proportion of elderly people in society increases.
- Lower tolerance towards therapy in elderly people.

How common are different cancer types?

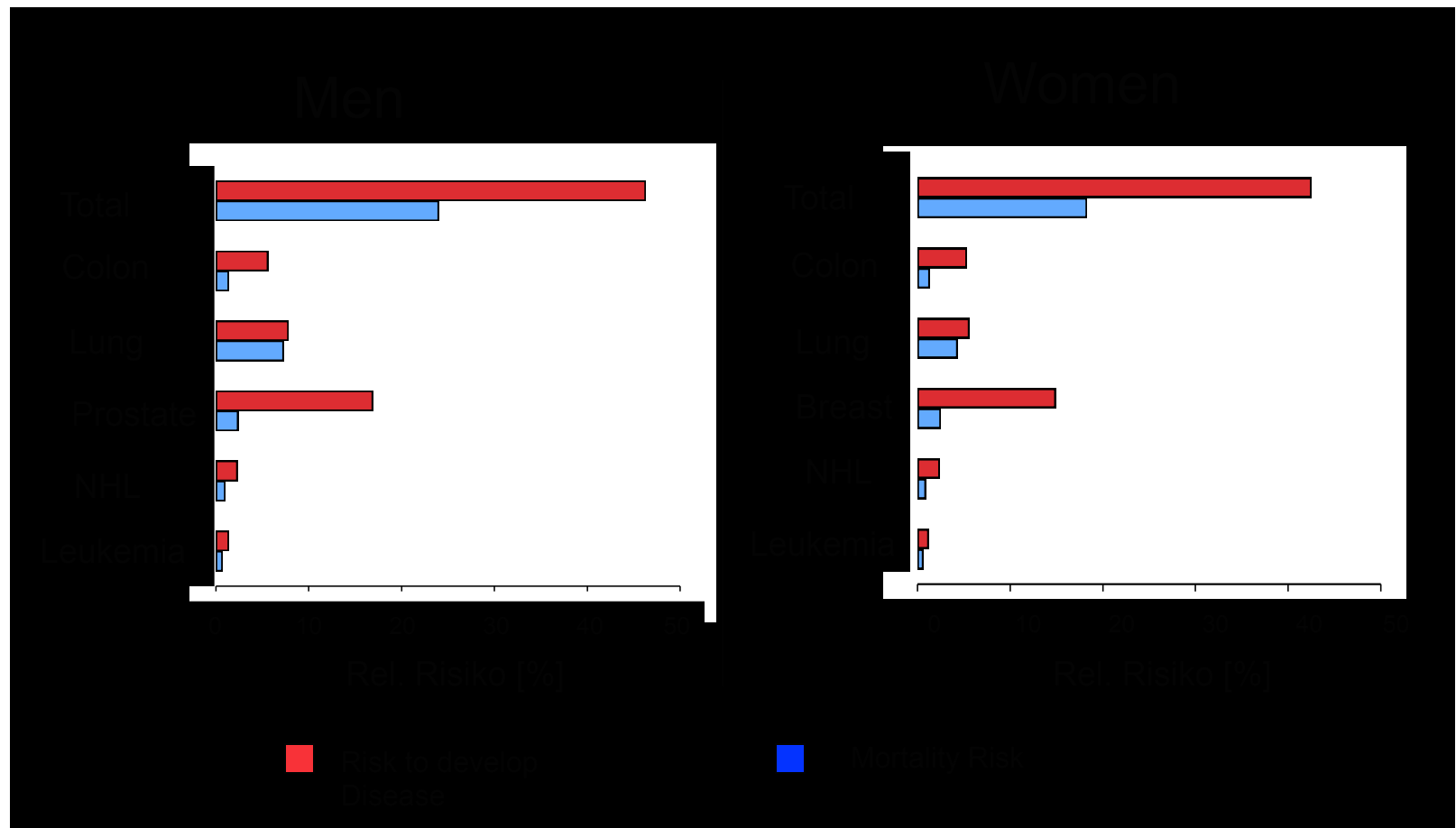
2007 Estimated US Cancer Cases*



*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.
Source: American Cancer Society, 2007.

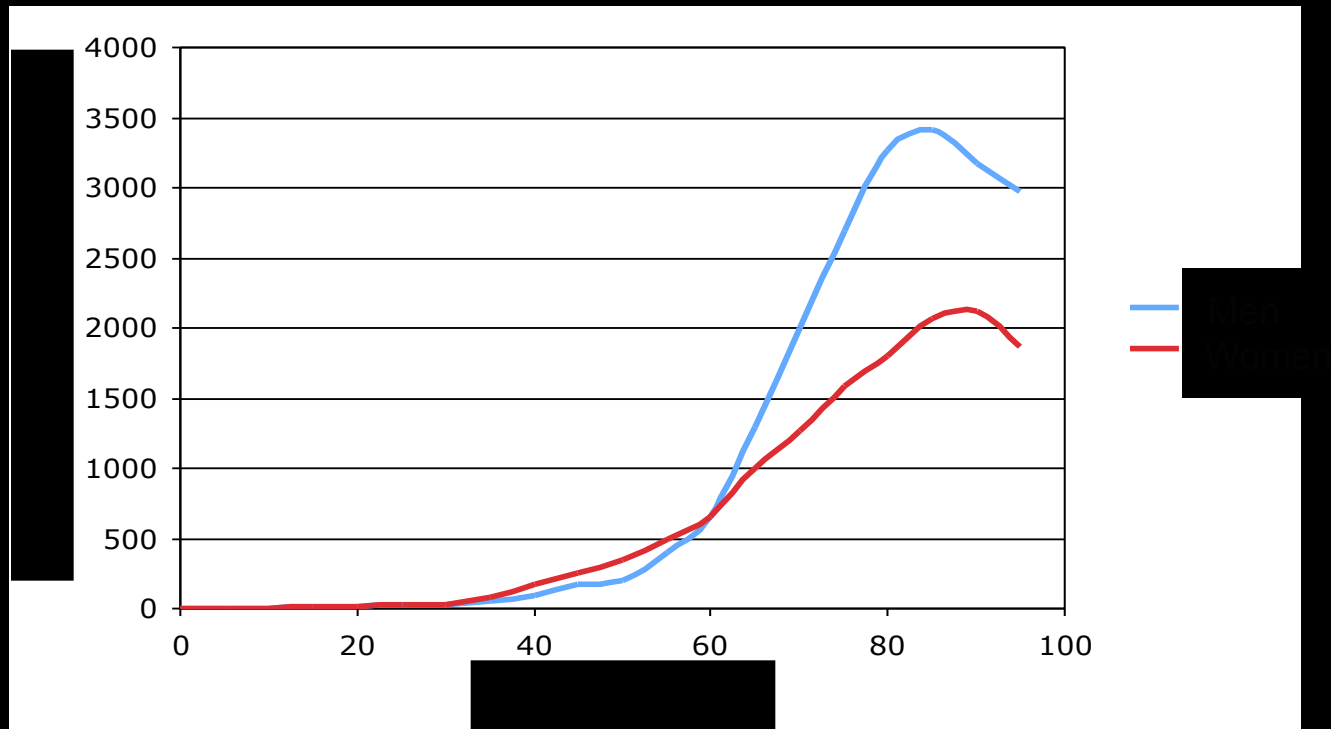
Relative Risk, to develop cancer and to die of the disease

(USA 2006-2008)



Age Distribution of Cancer Incidence

(USA 2006-2008)



Average Life Expectancy

At an Age of	Women	Men
70	15 y	11 y
75	12 y	9 y
80	9 y	7 y
85	7 y	6 y

Overview of covered topics

- Imaging Modalities in Cancer Diagnosis
- Principles of the Biology of Cancer
- Principles of Cancer Therapy
- Mechanis of Action of Novel Cancer Therapeutics
- Cost of Therapy

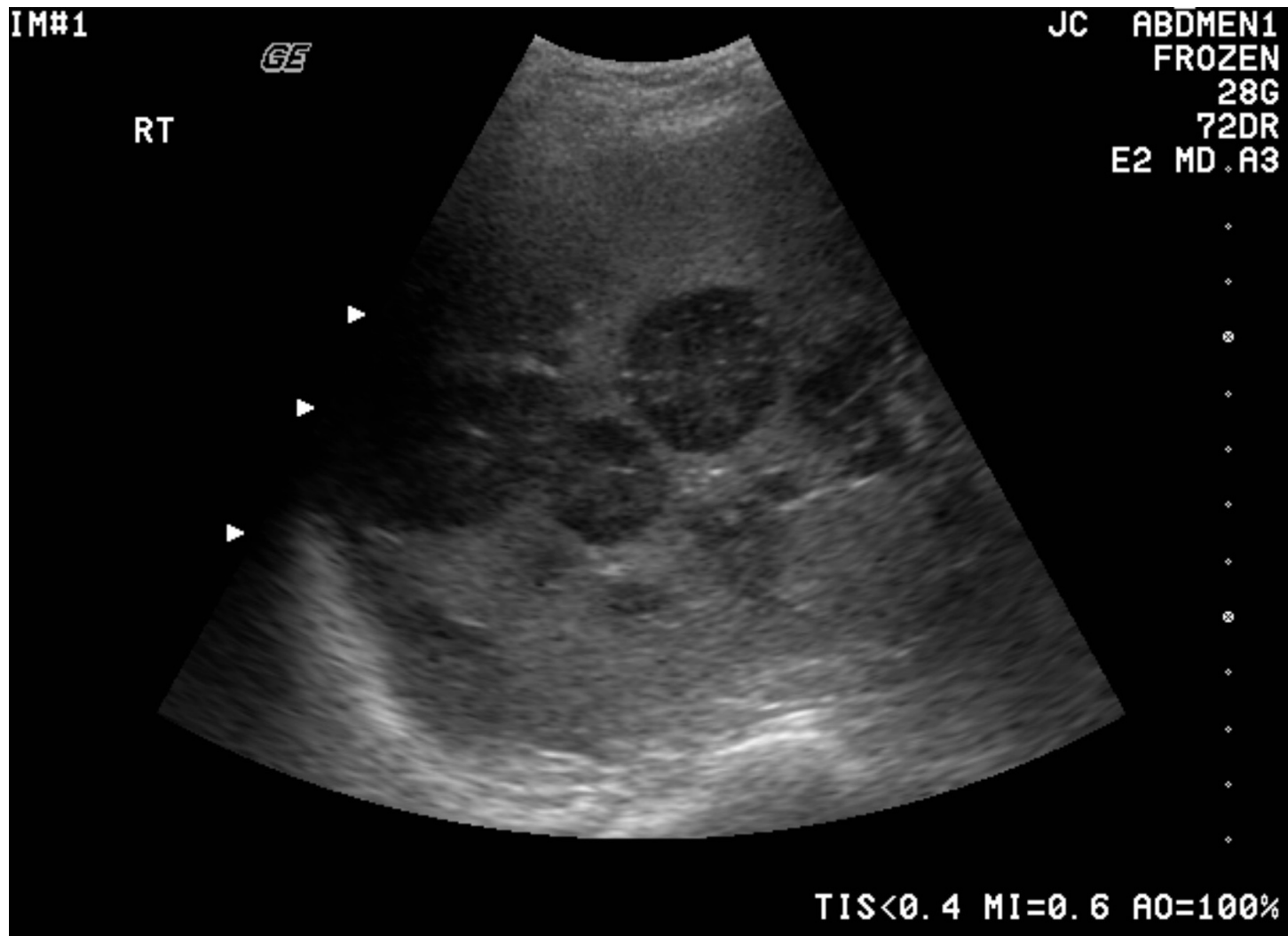
Diagnostic Modalities

- Classic X-Ray (1895)
- Ultrasound (1942)
- Computed Tomography/CT (1971)
- Magnetic Resonance Imaging/MRI (1985)
- **P**ositron-**E**mission-**T**omography/PET (1975)
- PET-CT (2000)
- PET-MRI (2009)

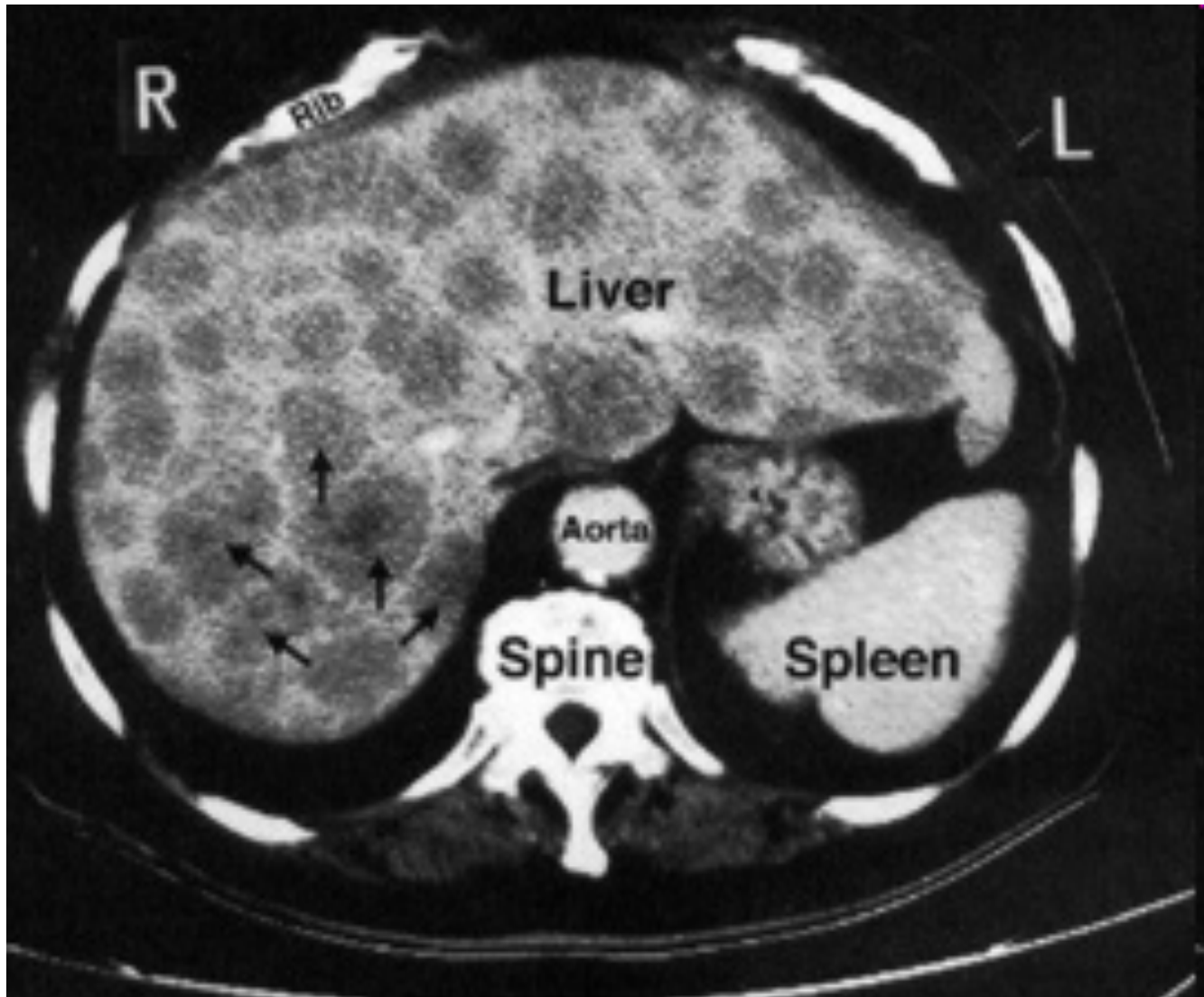
Chest X-Ray



Ultrasound Exam of Liver



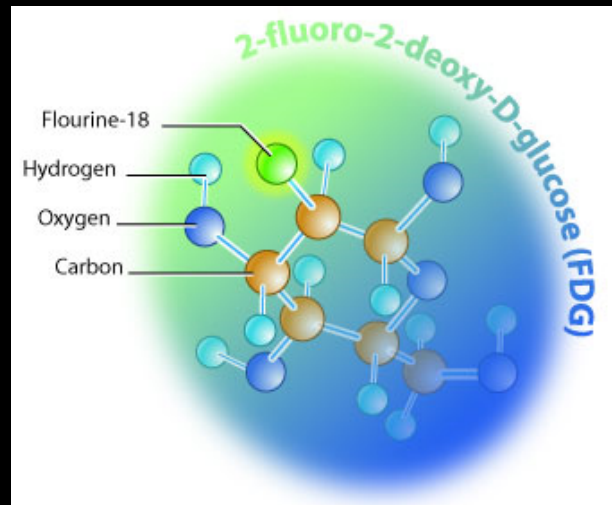
CT Scan



Hybrid Imaging Techniques

CT/MR Morphology/Anatomy

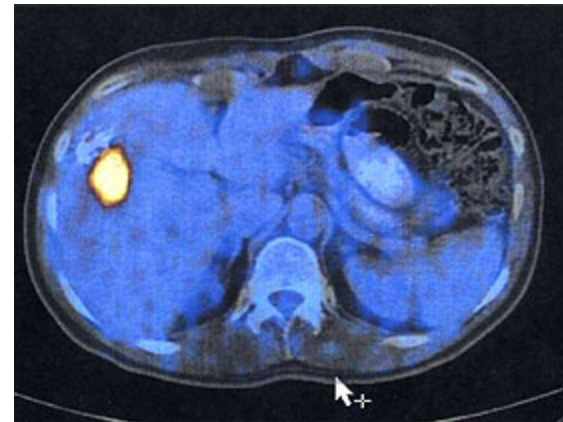
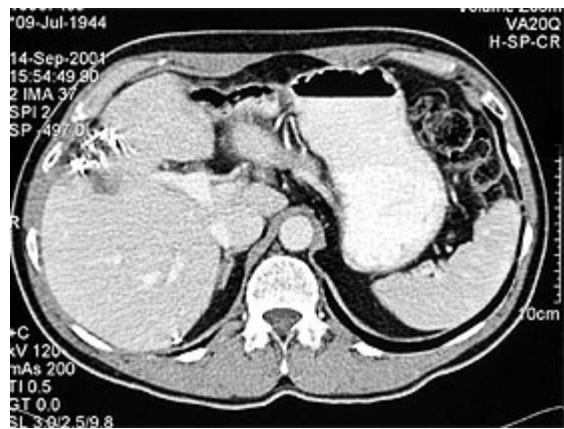
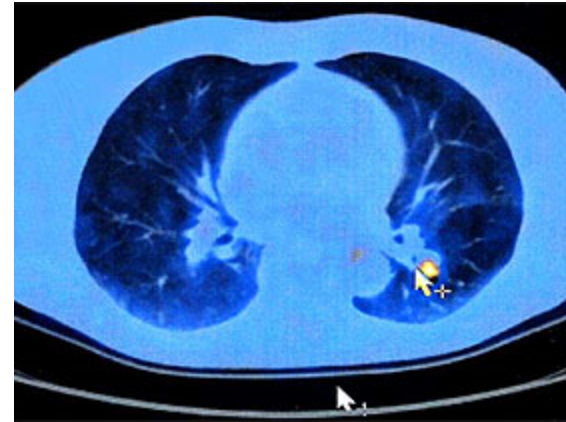
PET Metabolic Activity of Tissue



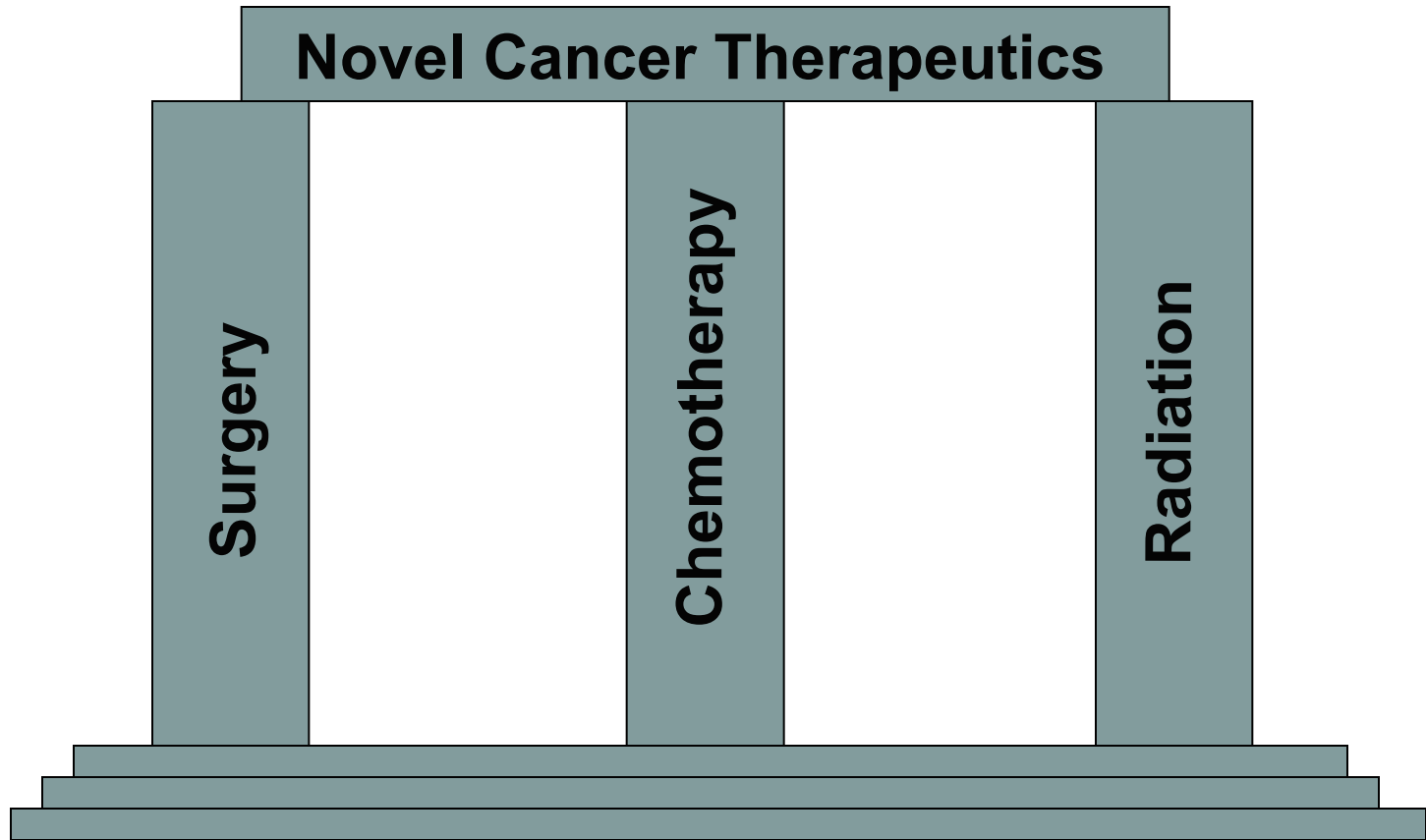
CT



PET-CT

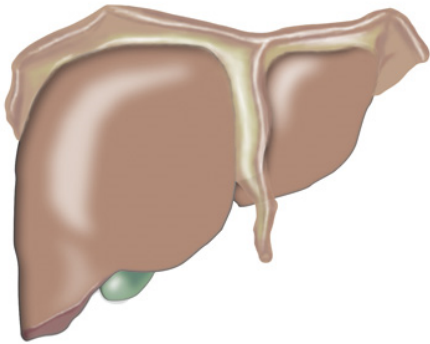


Pillars of Tumor Therapy

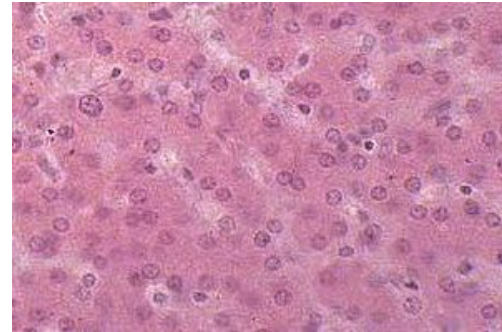
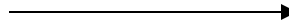


Understanding the biological principles of tumor growth is essential to be able to advance cancer therapy.

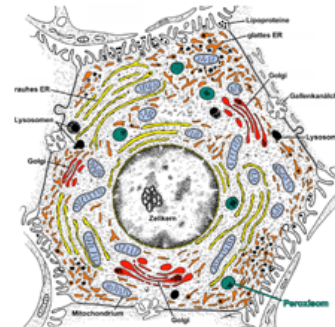
Organ → Tissue → Cell



Liver

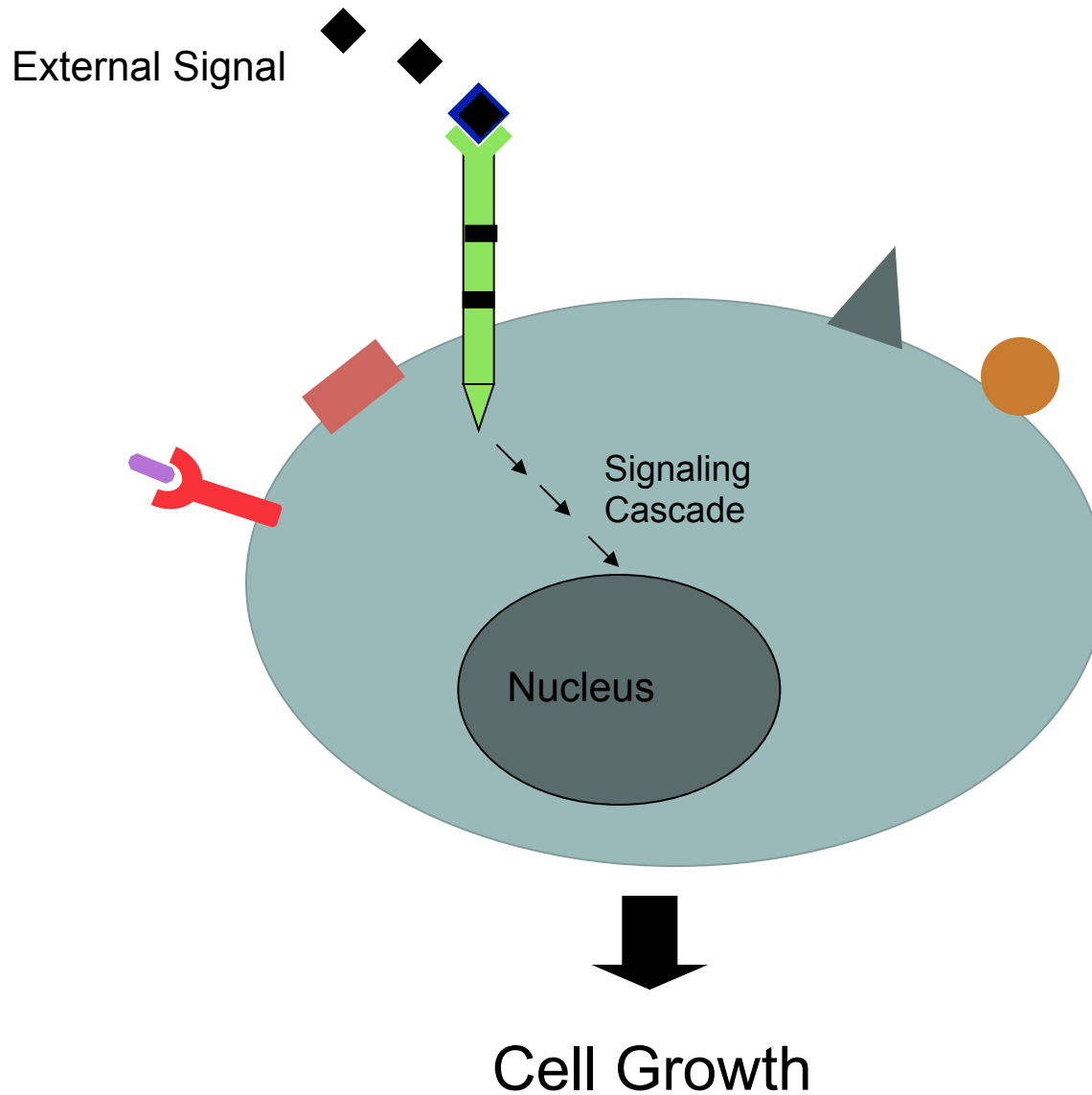


Liver Tissue

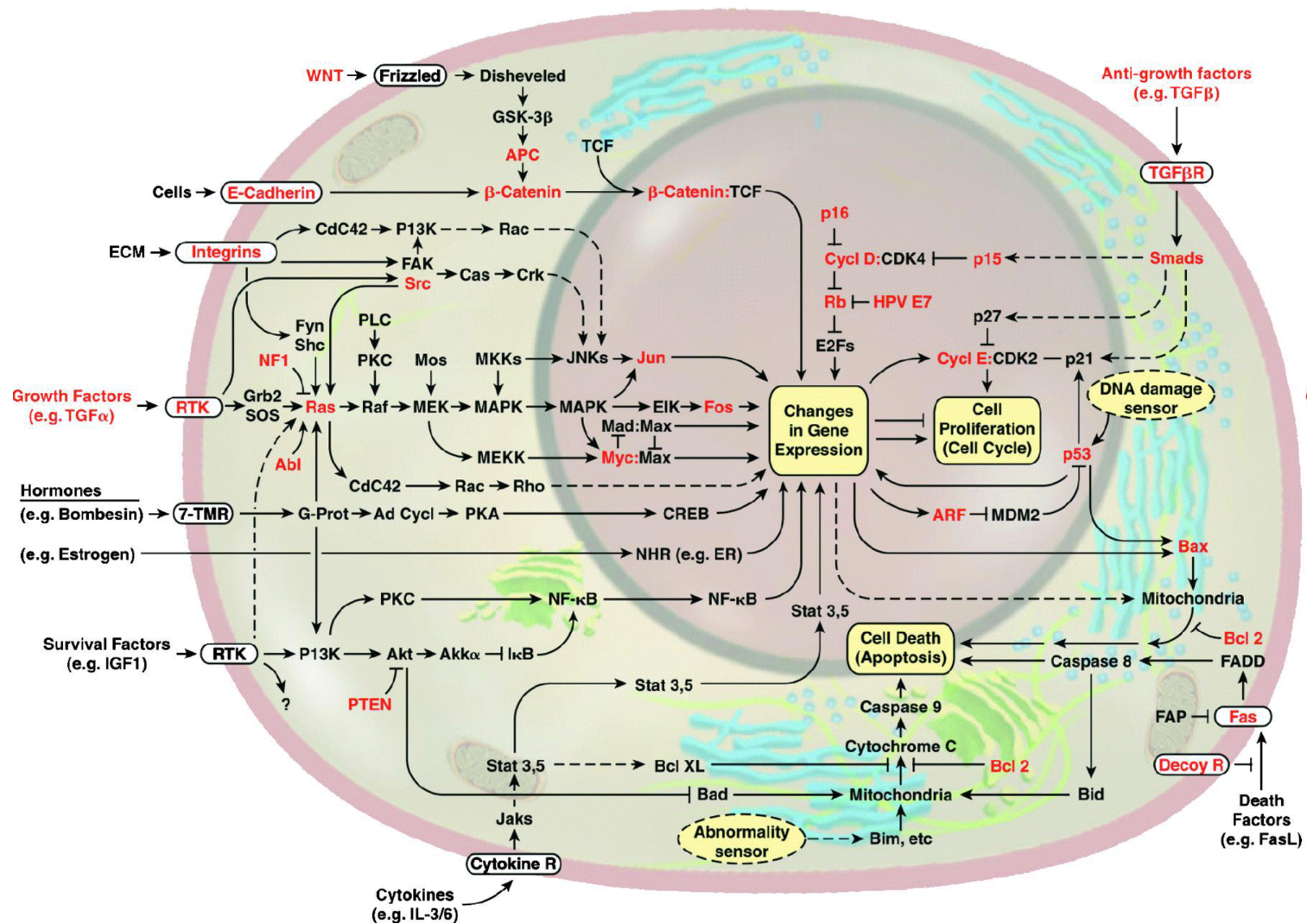


Liver Cell

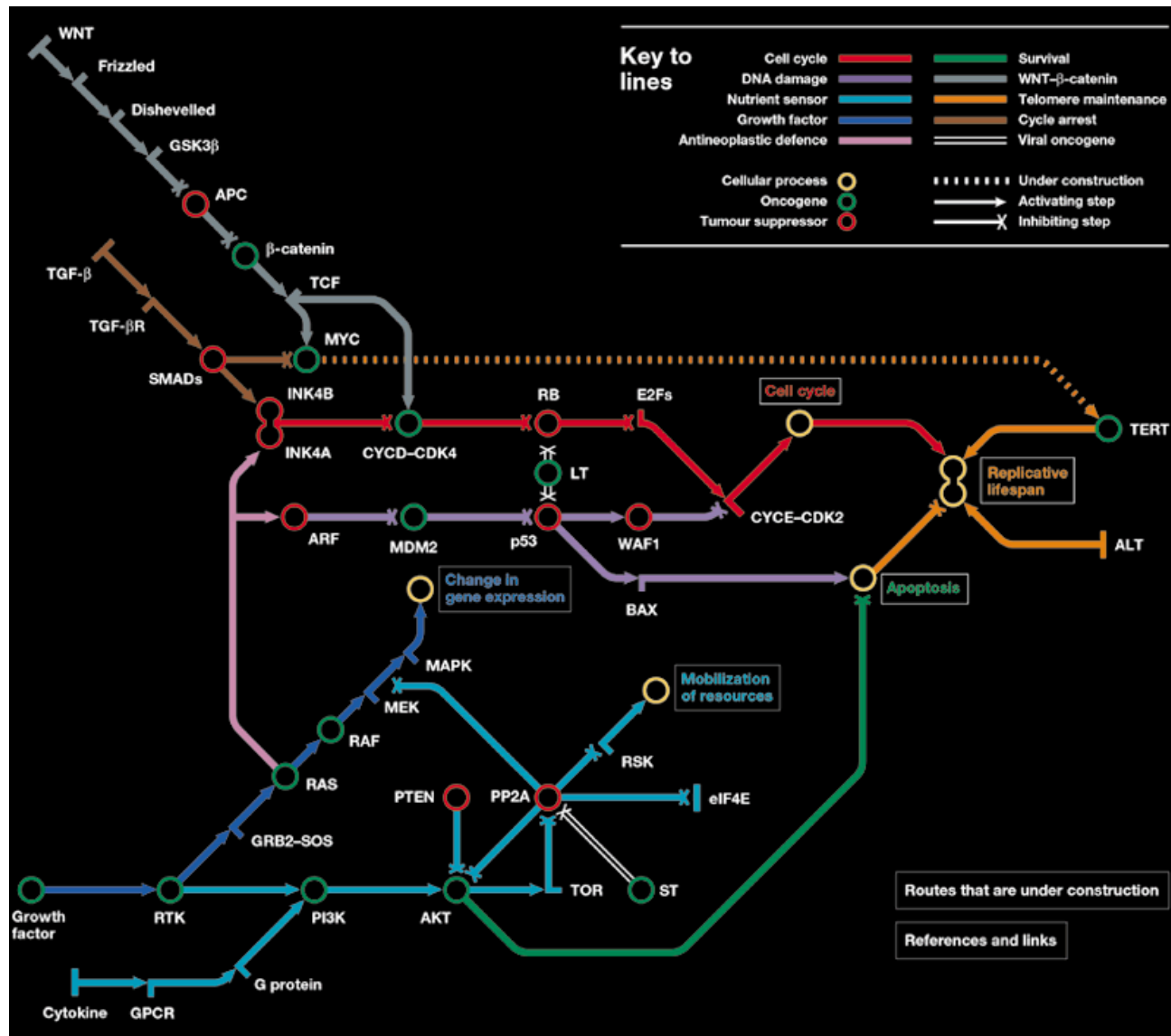
Healthy Cell



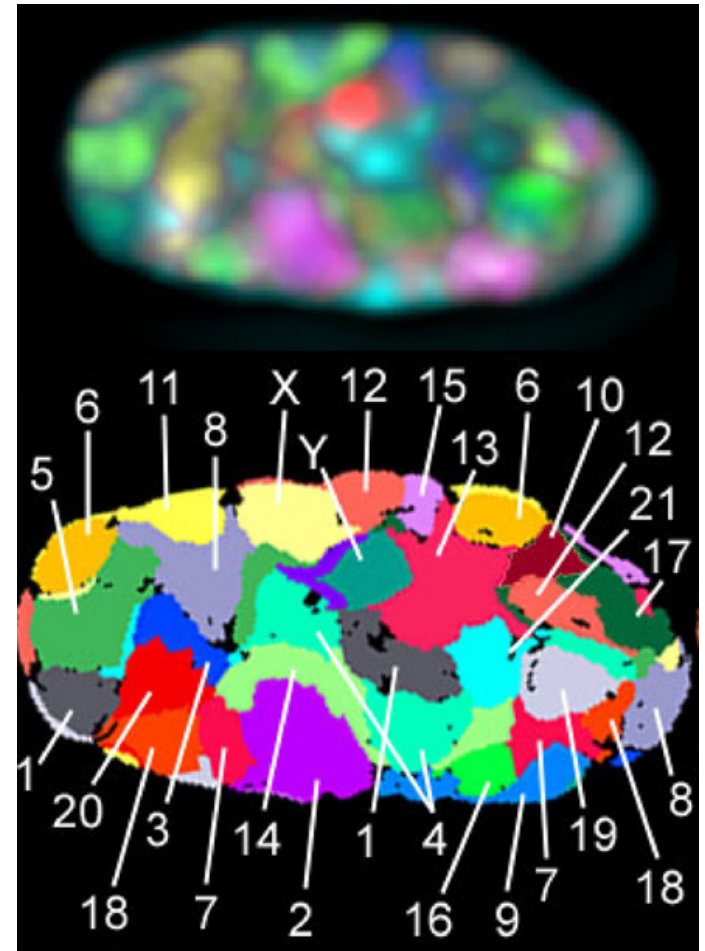
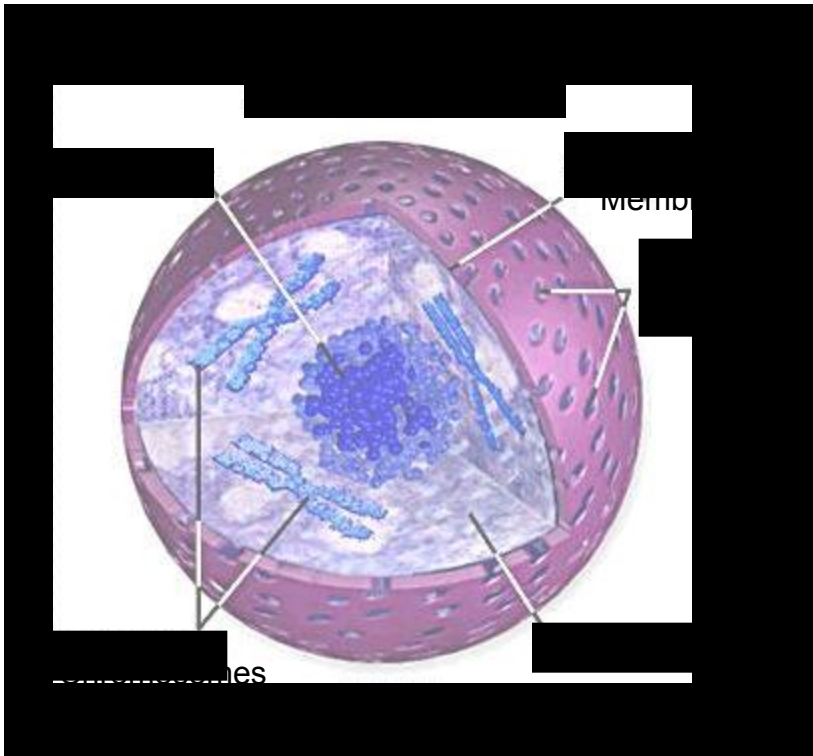
Signal Transduction Pathways in a healthy cell.



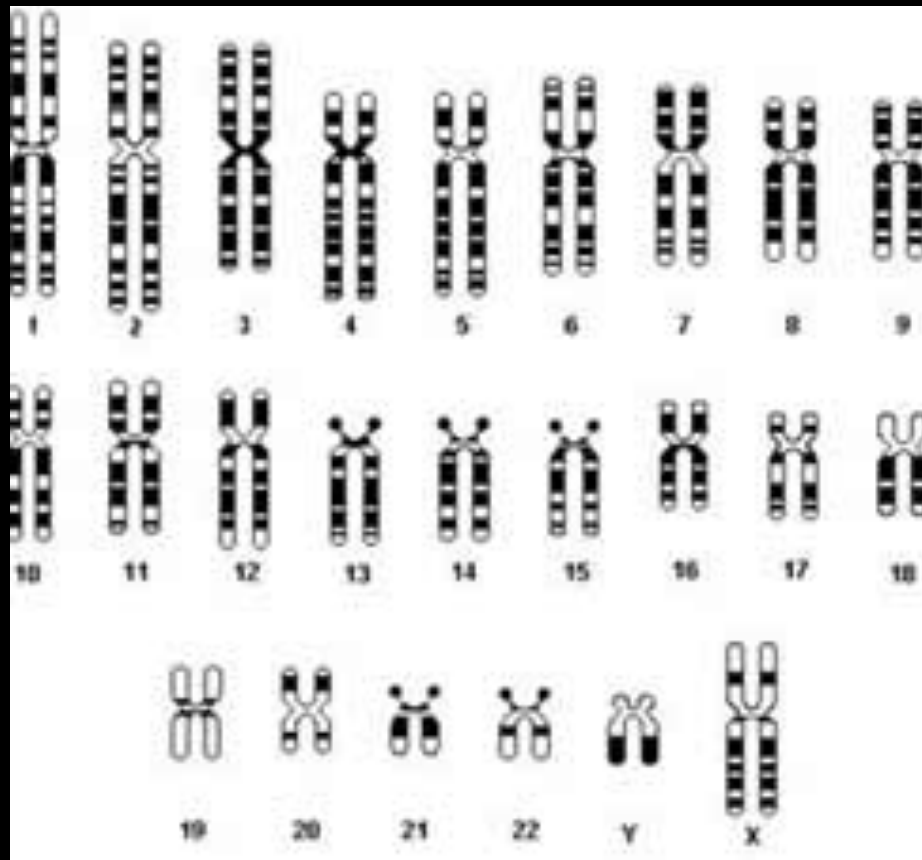
A subway map of cancer pathways



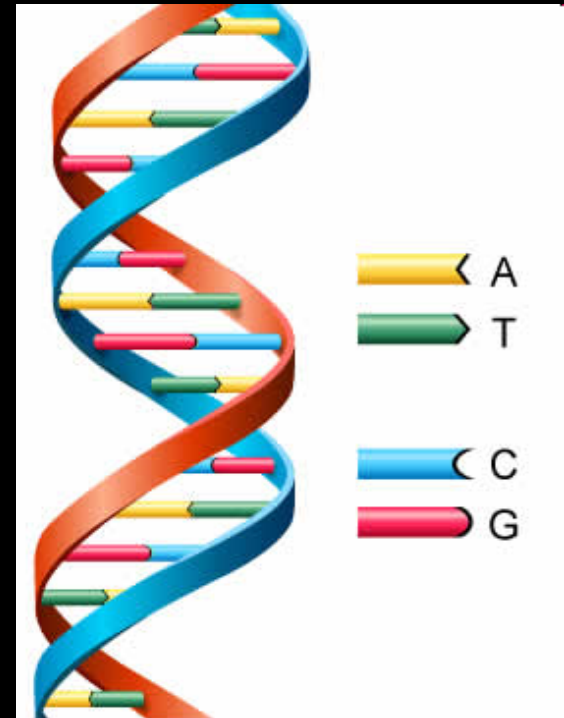
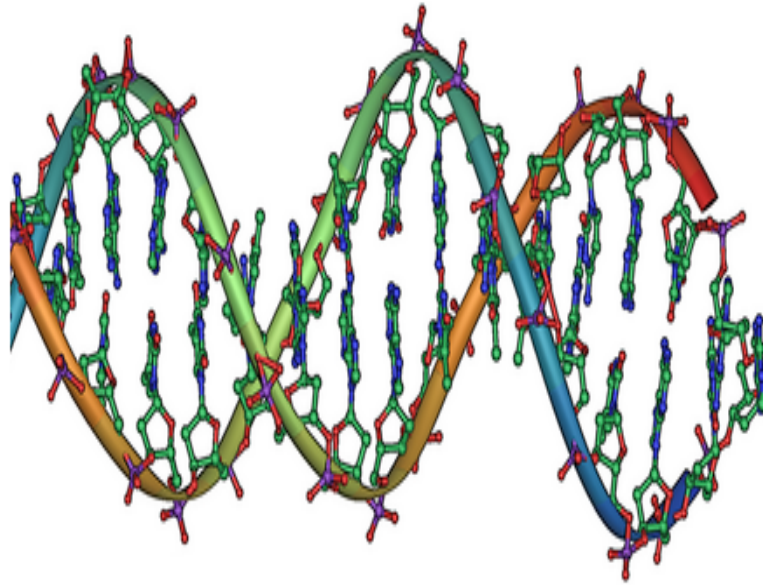
Cell Nucleus



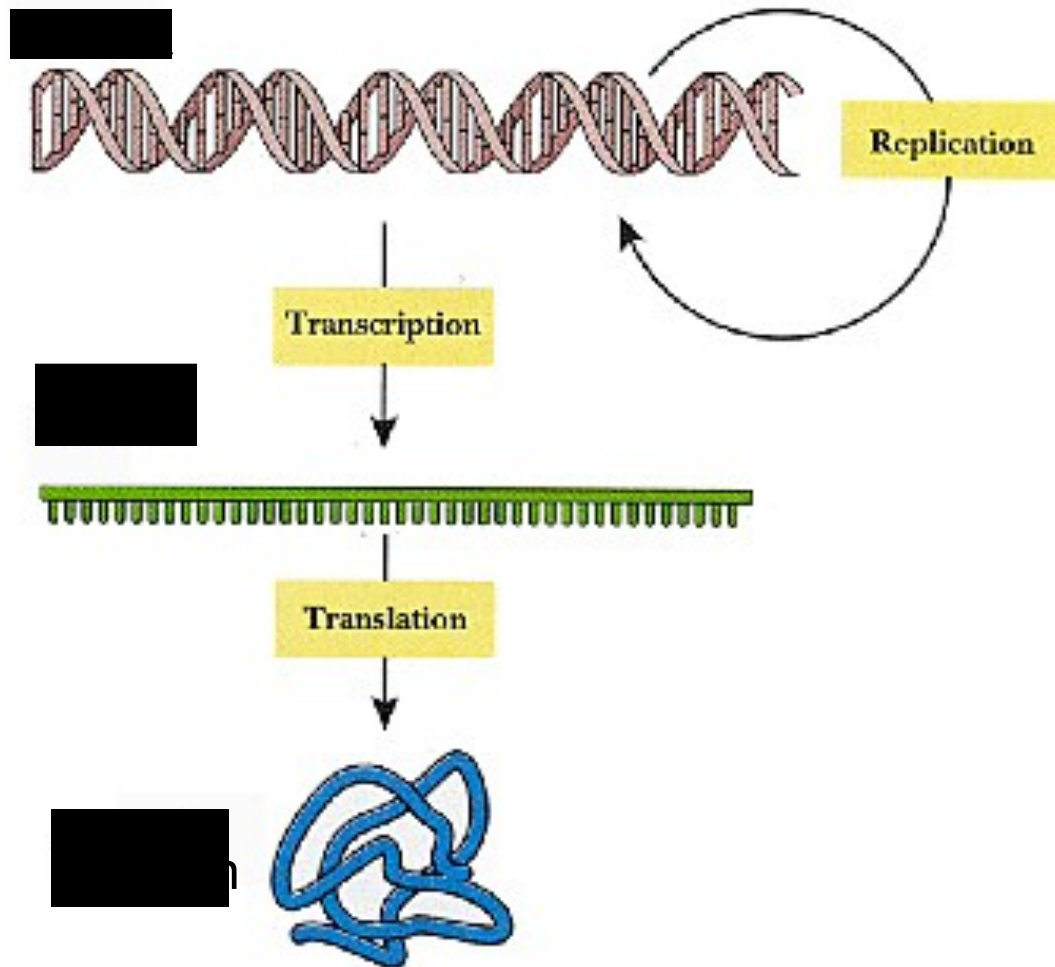
Chromosomes of a Healthy Cell



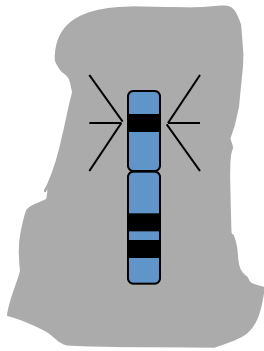
DNA Double Helix



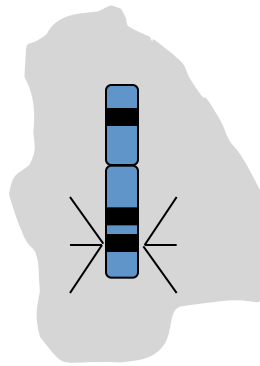
Protein Biosynthesis from DNA



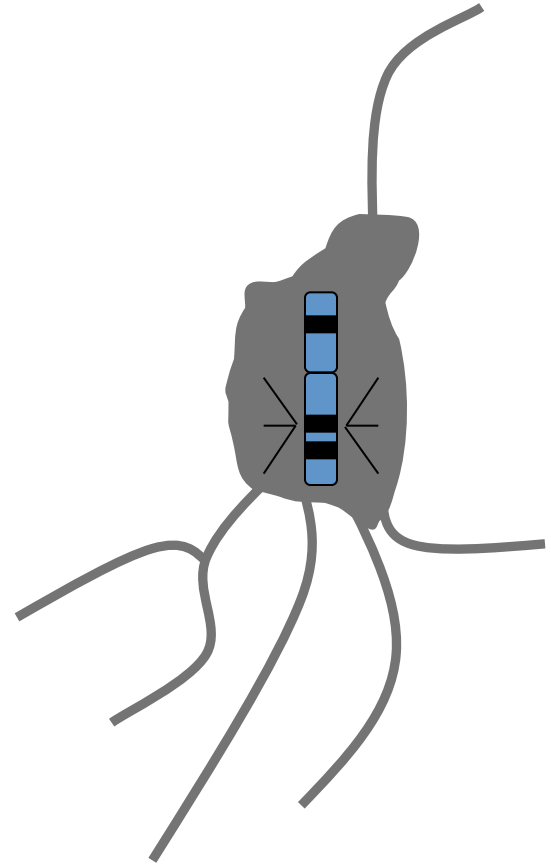
Activation of different Genes in Cells from different Tissues.



Hepatocyte

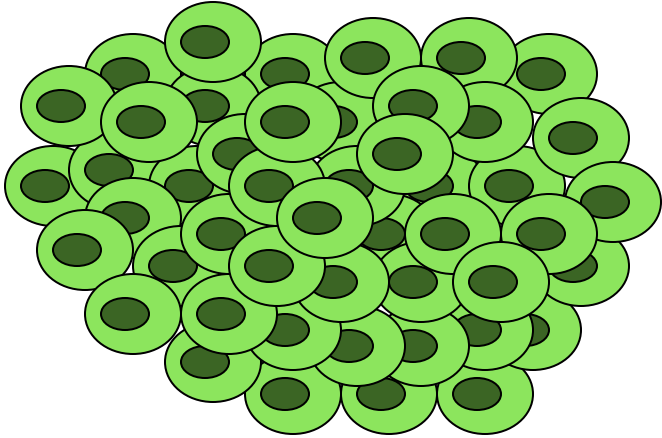


Osteoblast



Neuron

Healthy Tissue

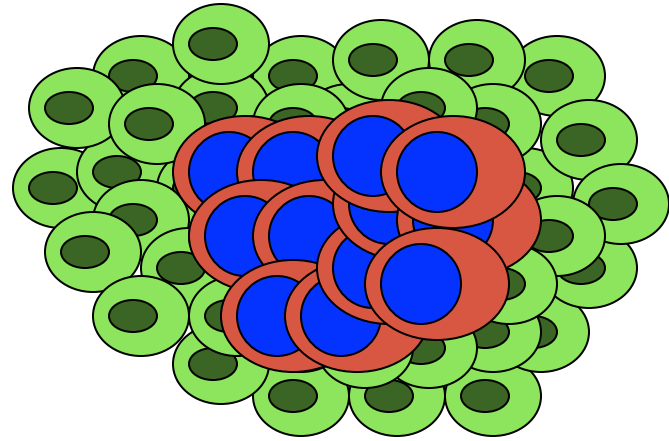


Intact DNA



Regulated Growth

Tumor



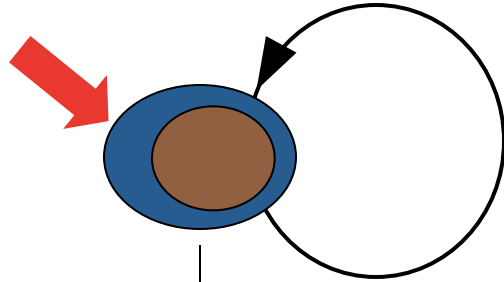
DNA Defect



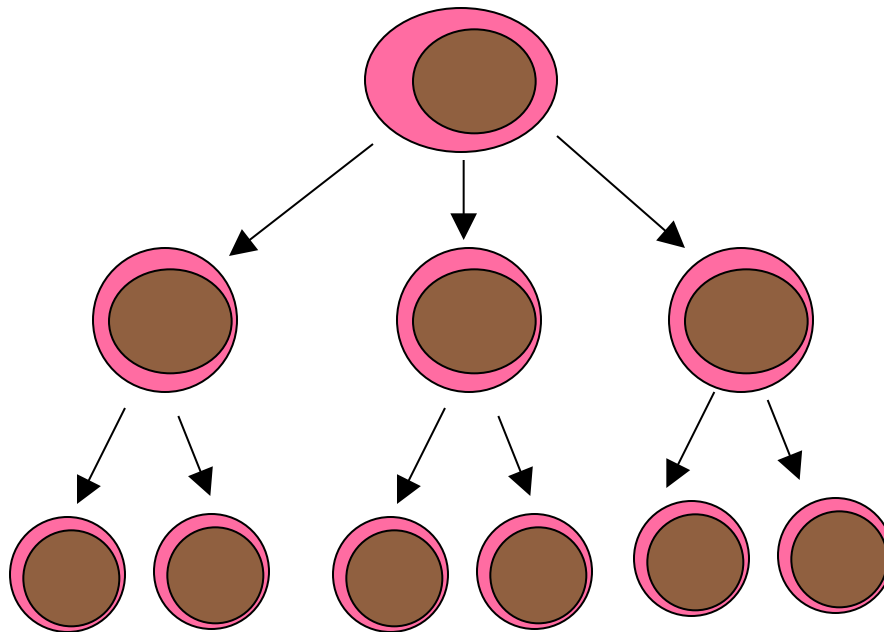
Deregulated Growth

Cancer is a DNA Disease

DNA Defect

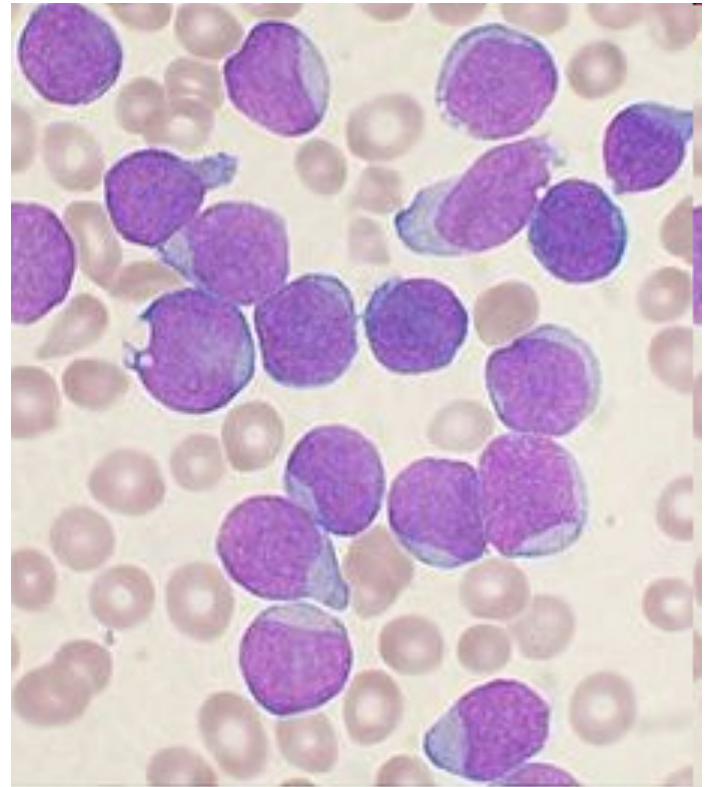


Tumor Stem Cell

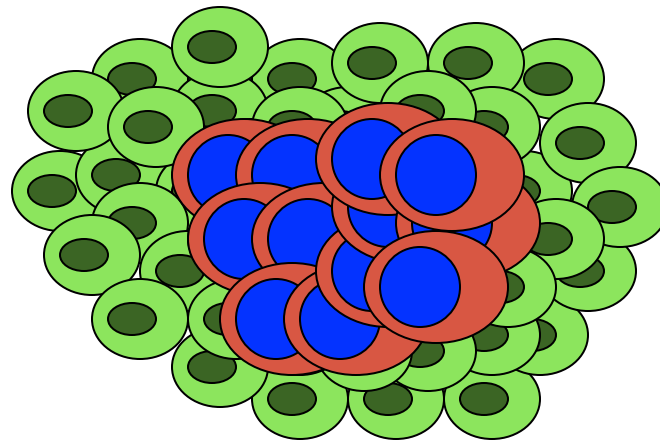


Tumor Cells

Leukemia

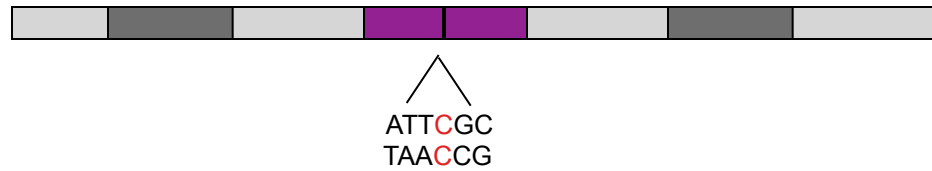


Tumor



DNA with Defect

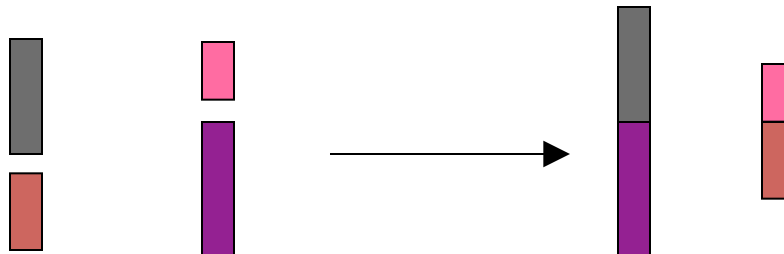
Mutation



Amplification

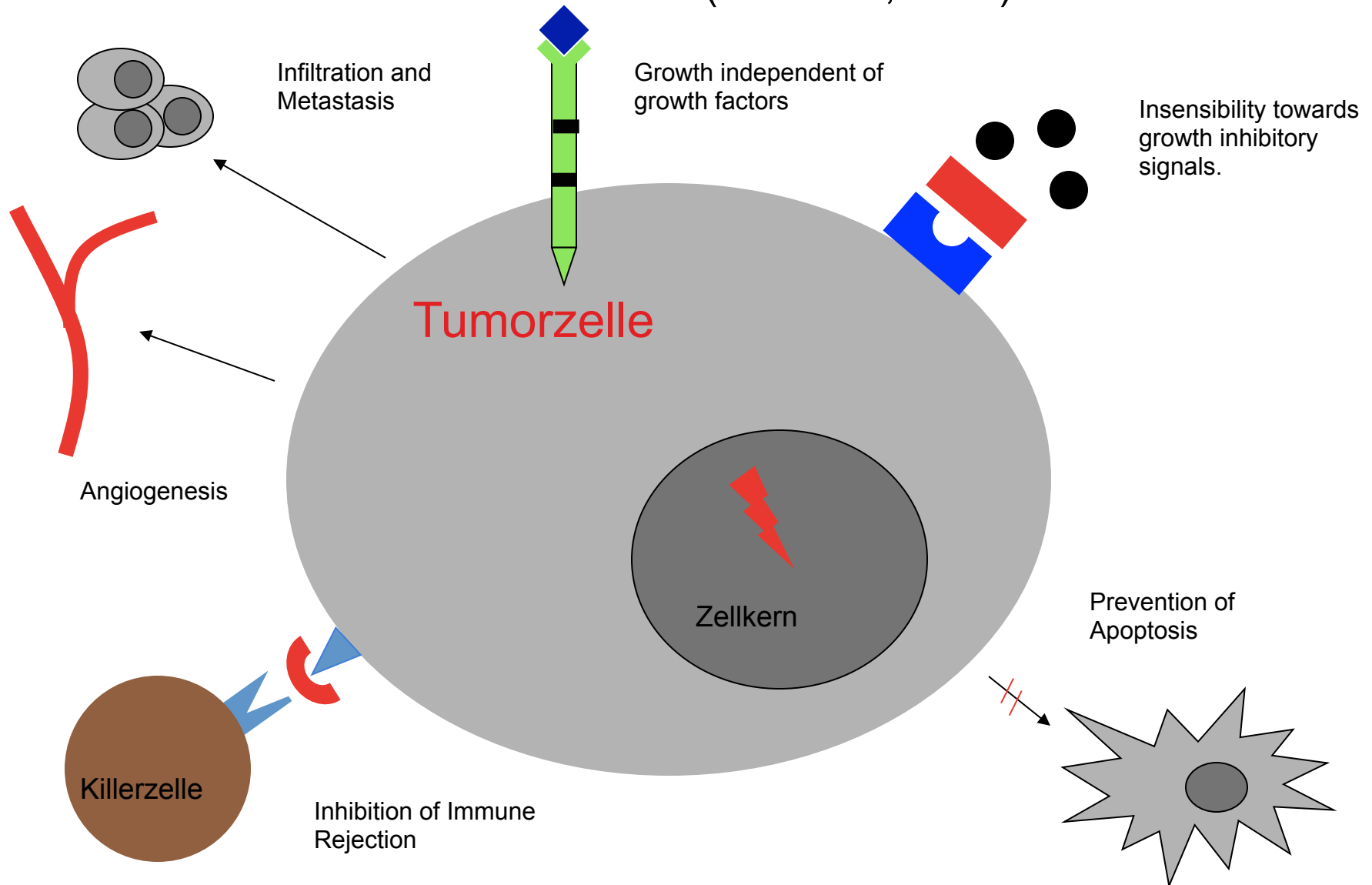


Translocation

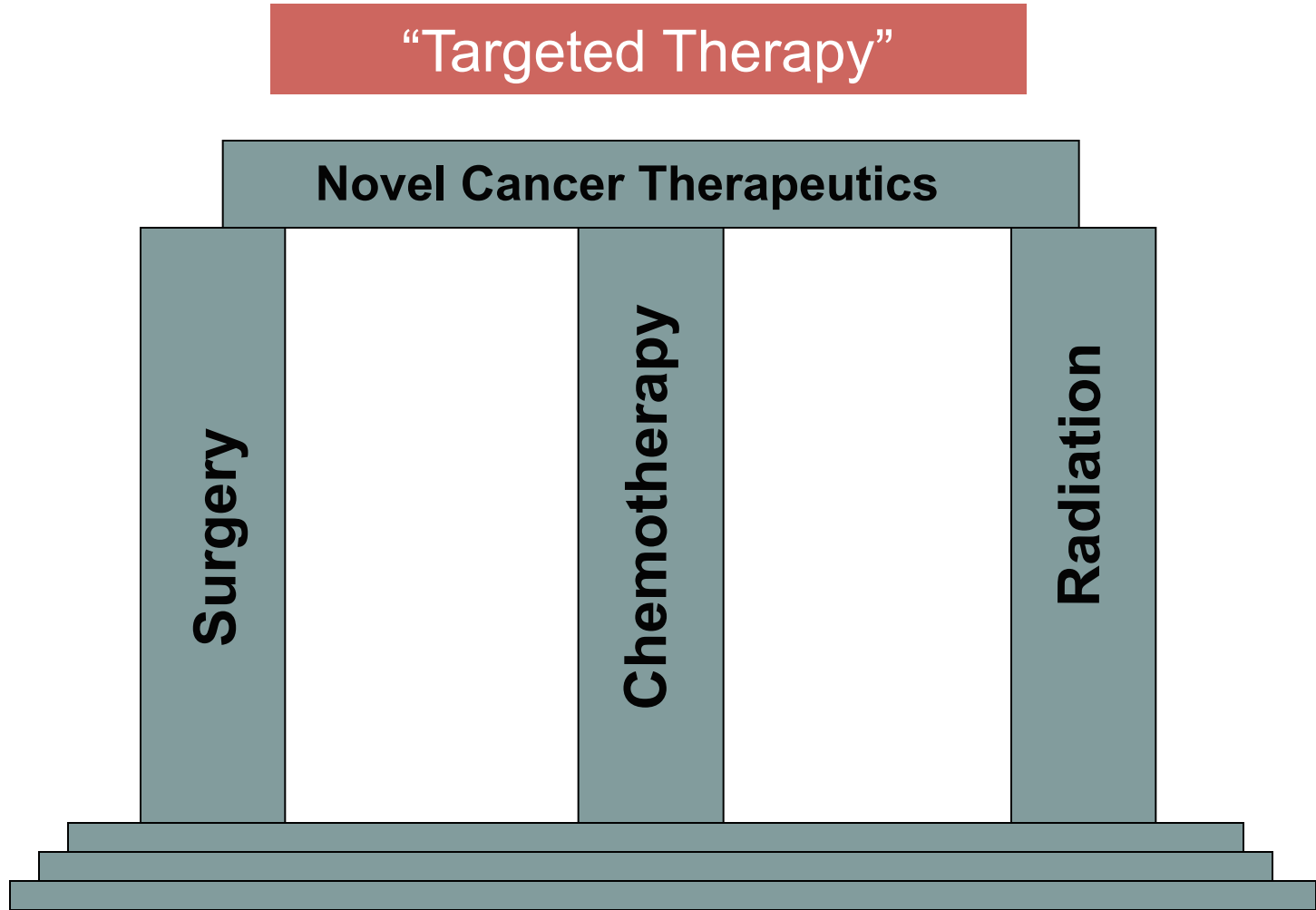


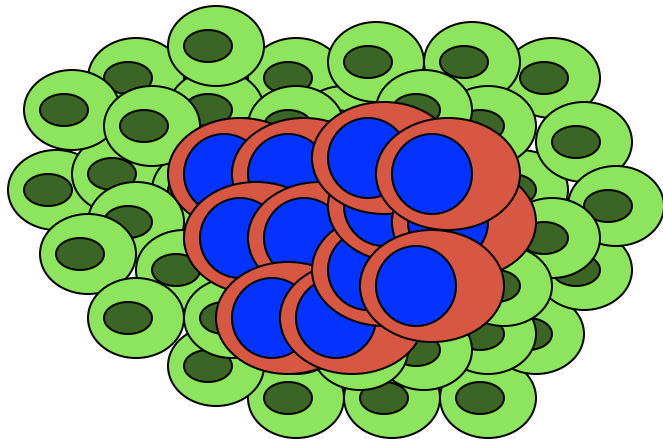
Consequences of a Genetic Accident

Six Hallmarks of Cancer (Hanahan, 2010)



Targetted Therapy of Cancer





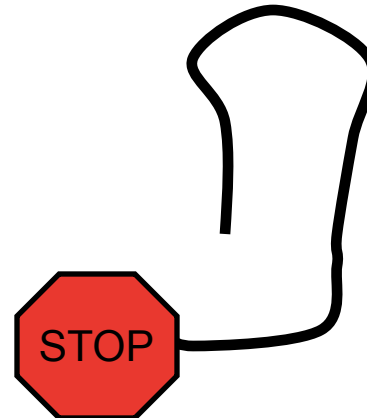
Tumor

DNA with Defect



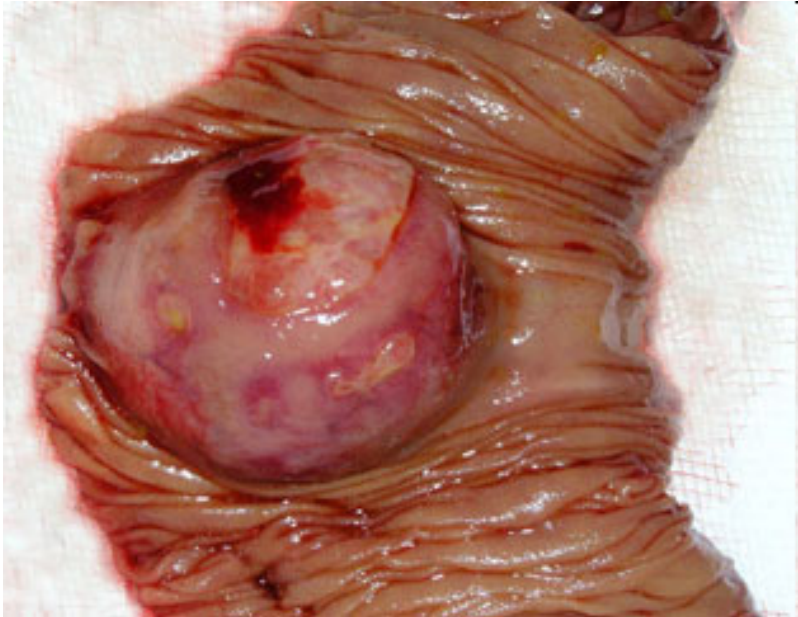
Deregulated
Growth

Gene Mutation

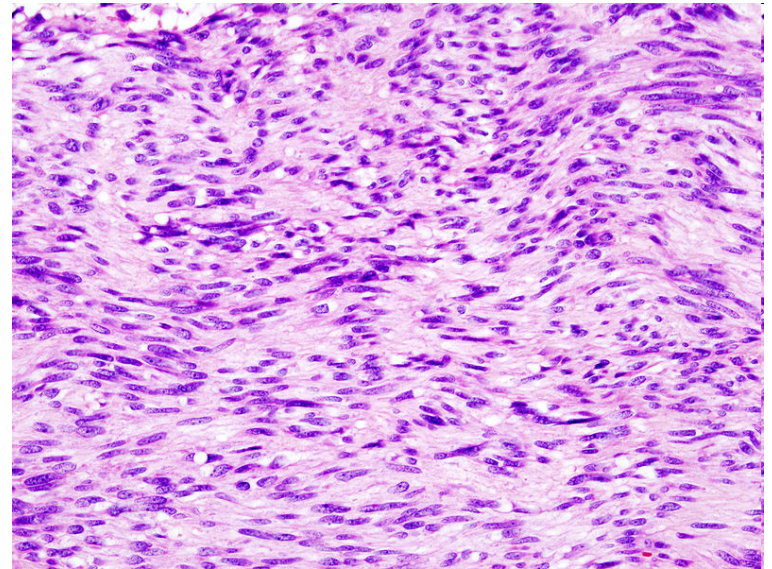


Protein with
Defect

Gastrointestinal Stroma Tumor (GIST)

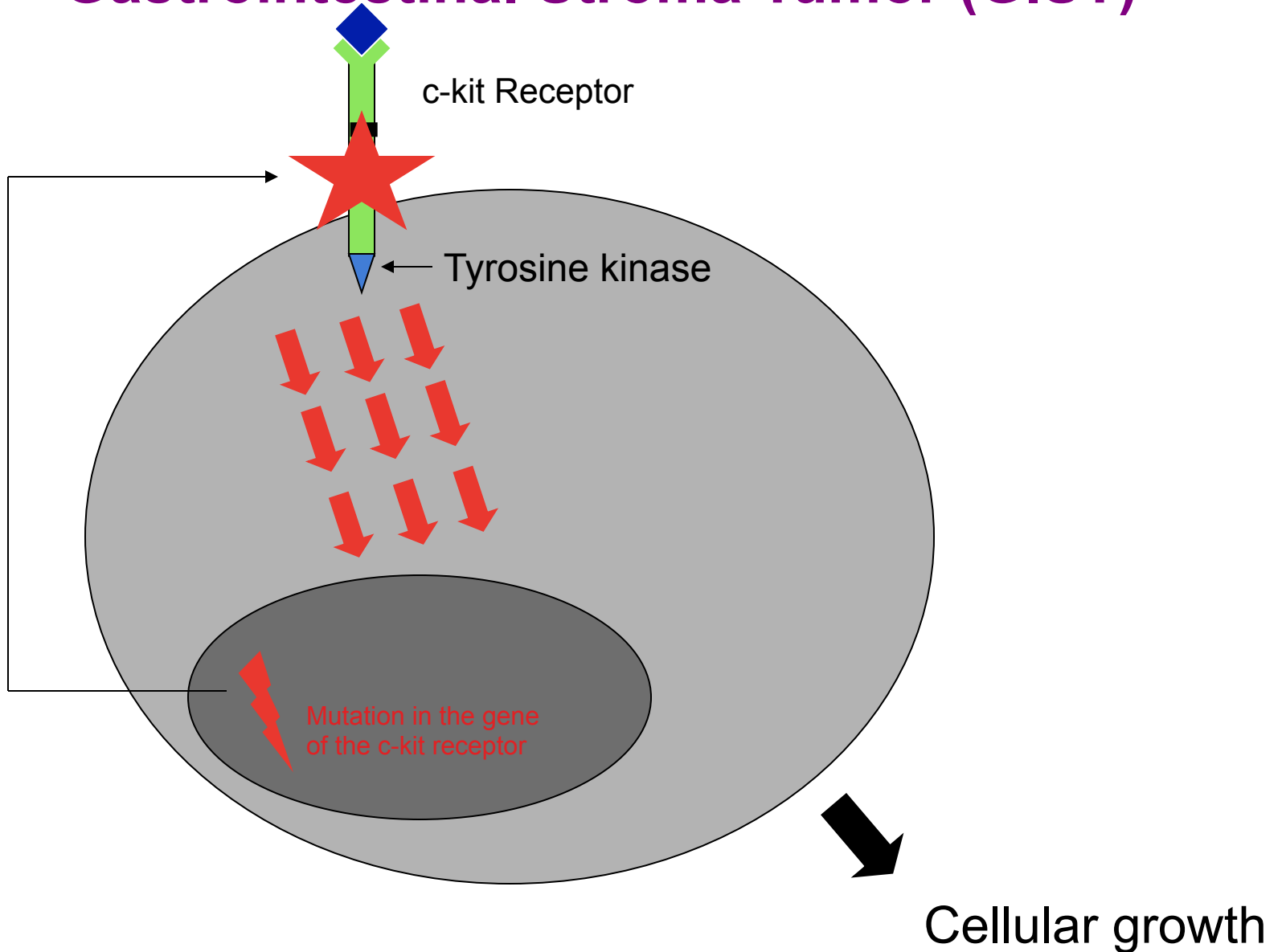


GIST of Small Intestine

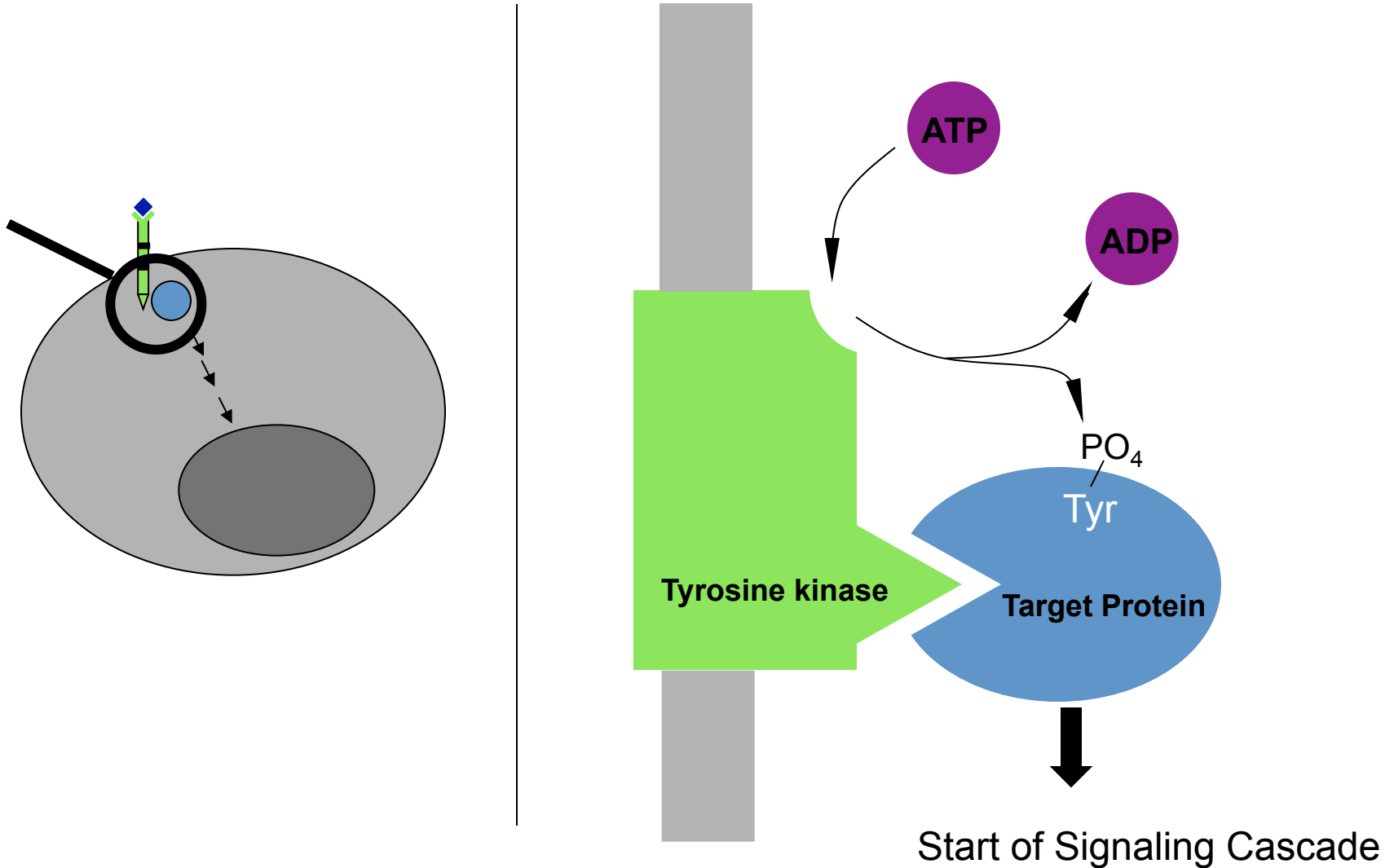


HE-Stain

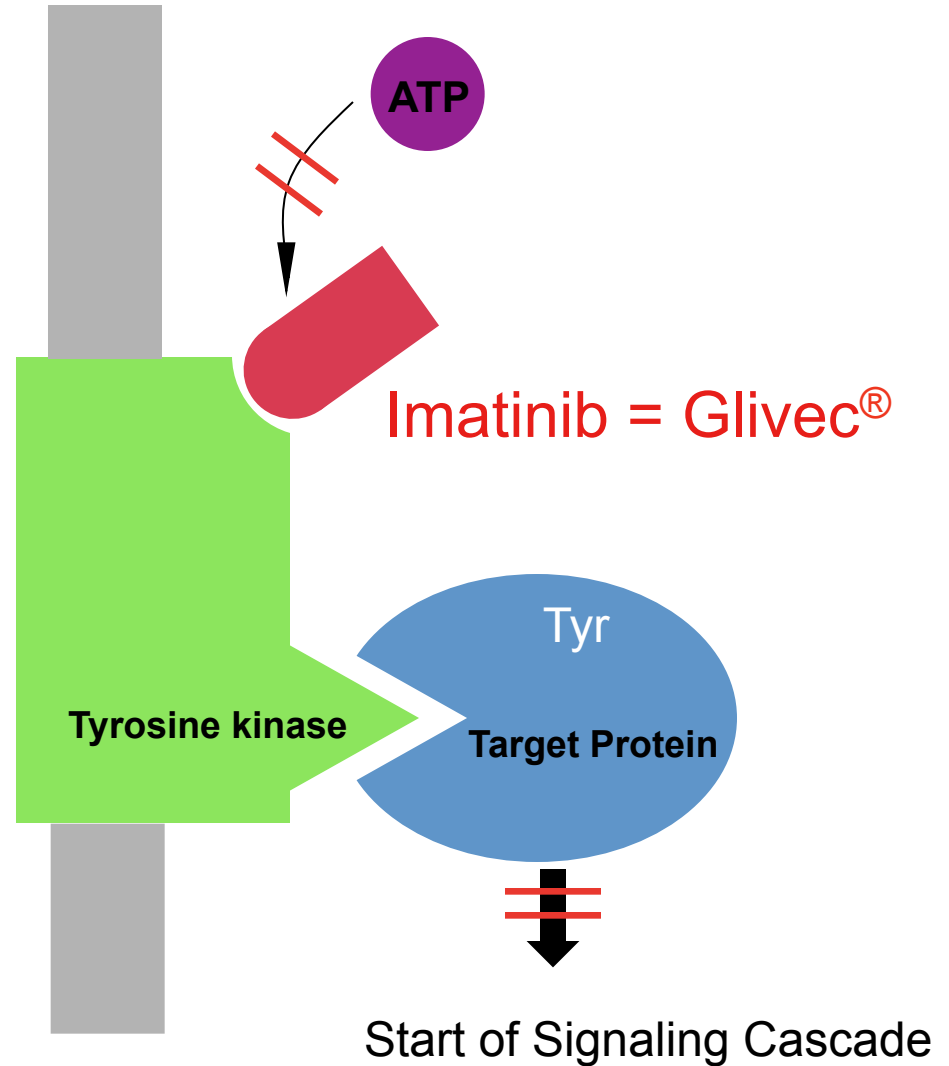
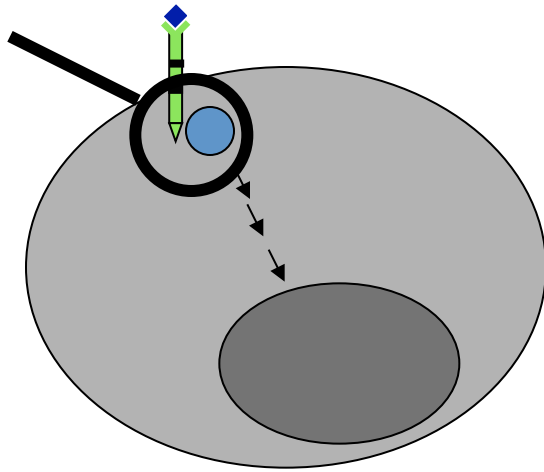
Gastrointestinal Stroma Tumor (GIST)



Mechanism of Action of a Tyrosine Kinase



Mechanism of Action of a Tyrosine kinase



Advanced Gastrointestinal Stroma Tumors (GIST)



Can be effectively treated for the first time !



Imatinib = Glivec®

Small Molecule

Gastrointestinal Stroma Tumor (GIST)

FDG-PET before and after a Therapy with Glivec®

Before Therapy



14 days later

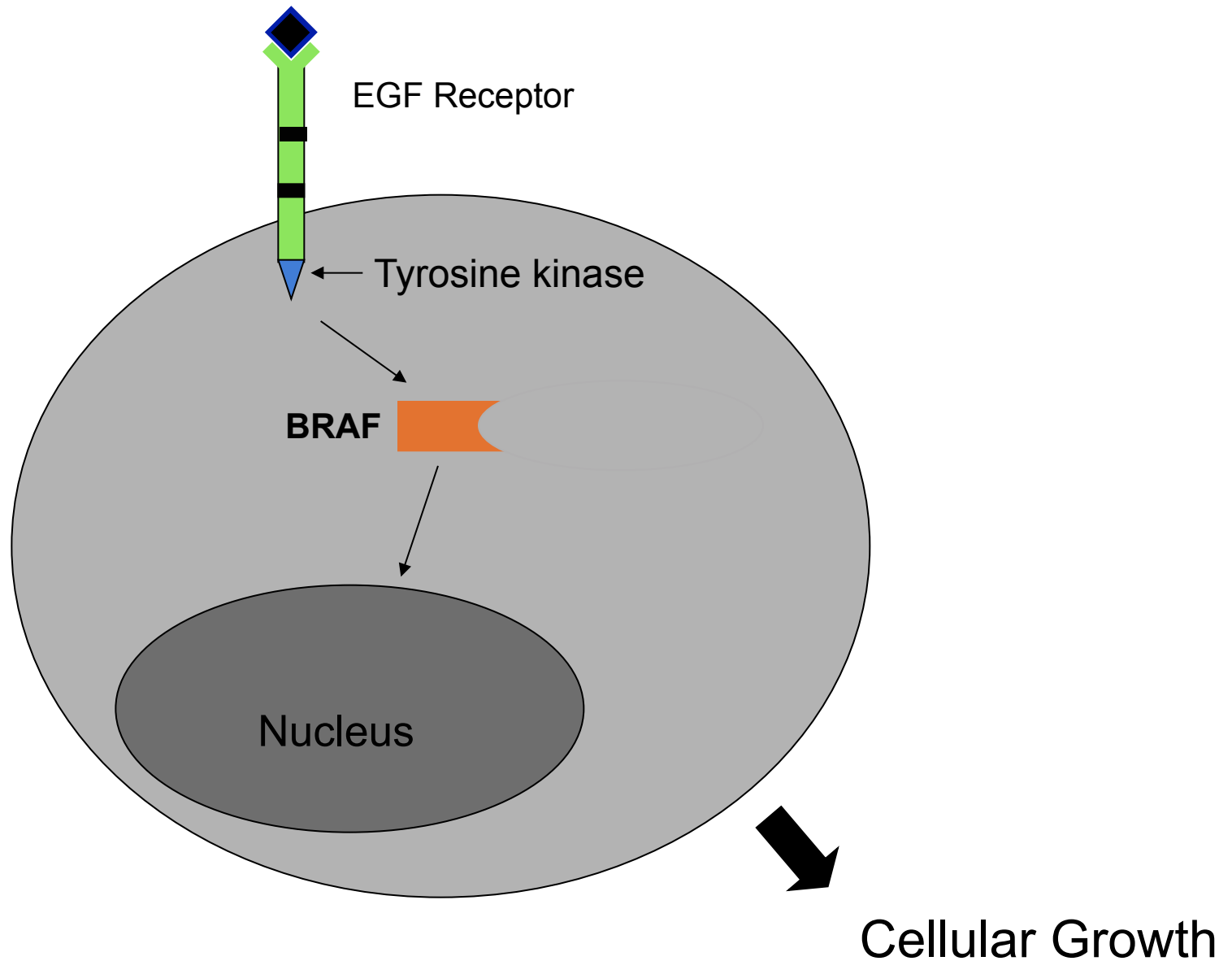


Malignant Melanoma

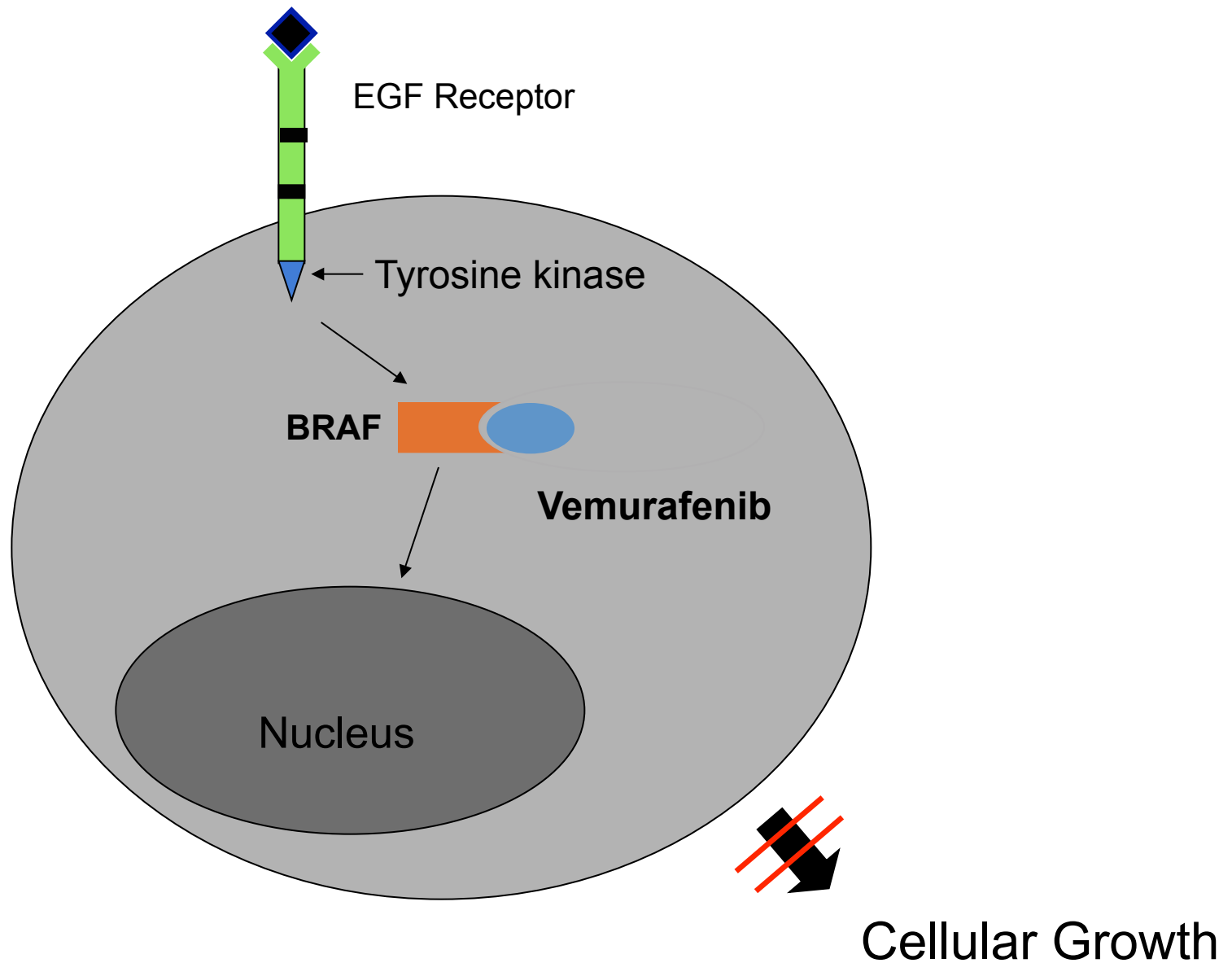


Median Survival: 6.4 Months

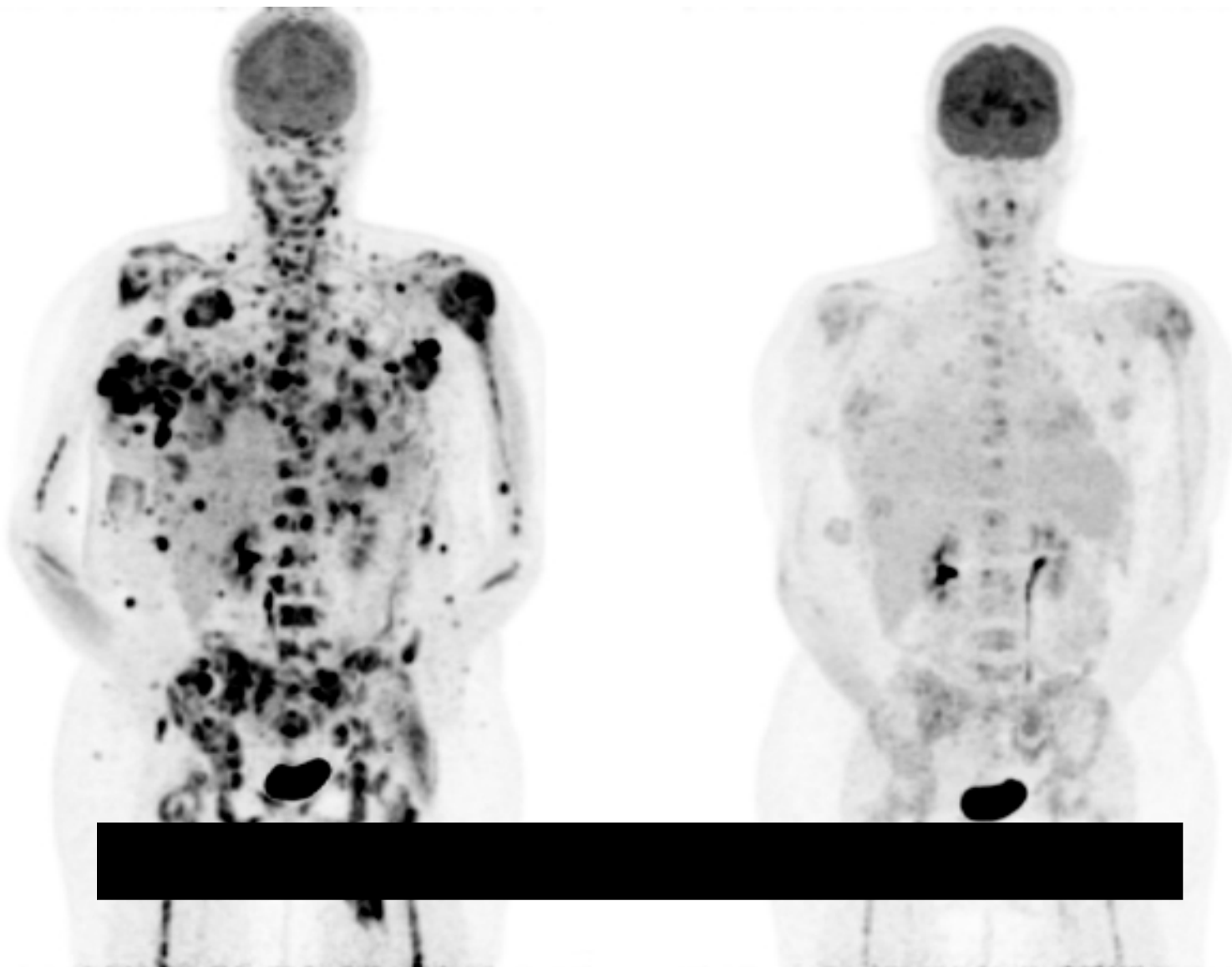
Malignant Melanoma



Malignant Melanoma



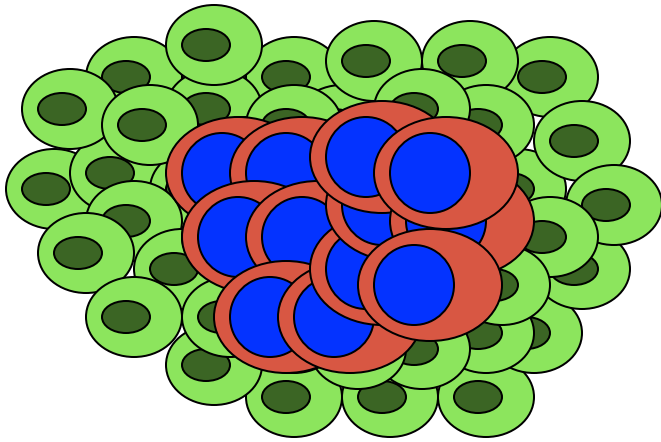
Treatment with Vemurafenib



Treatment with Vemurafenib

- First efficient innovation in the treatment of malignant melanoma in decades.
- Prolongation of Overall Survival from 6.4 Months to >10 Months.
- Certain Patients benefit much longer.
- Costs of Therapy > 100.000 €/year.

 Ethical Dilemma.



Tumor

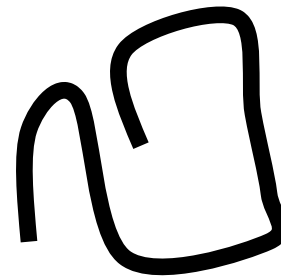
Gen Amplification



DNA with Defect



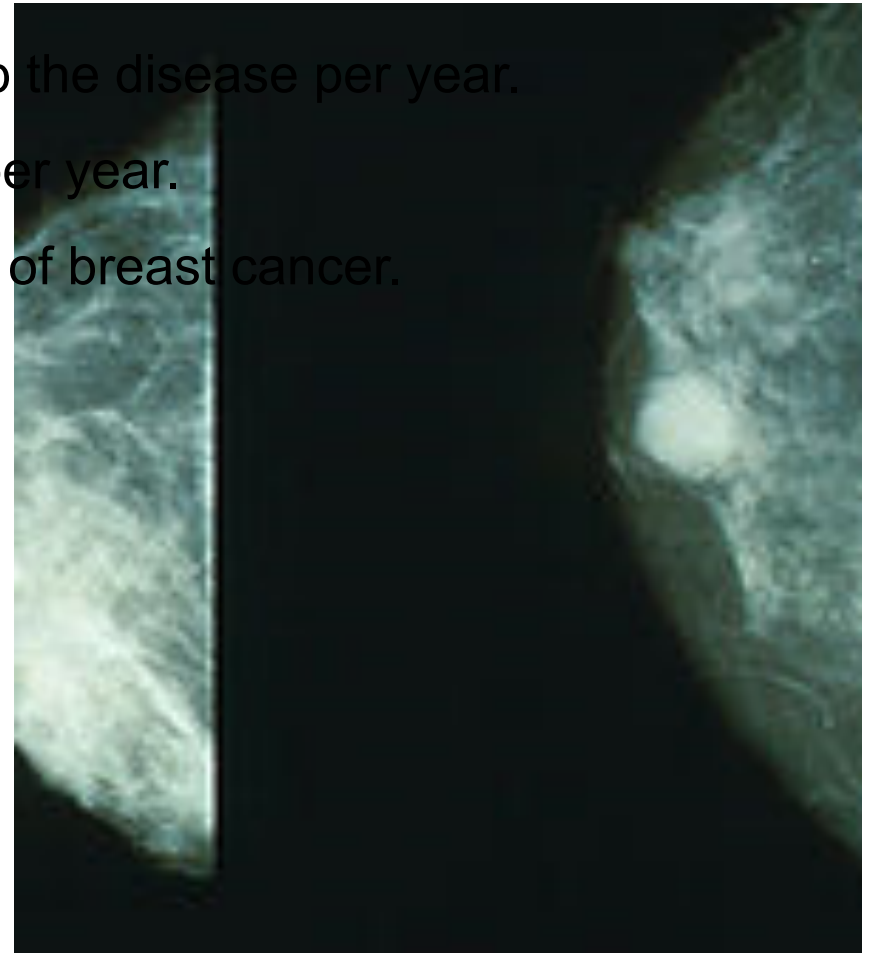
Deregulated
Growth



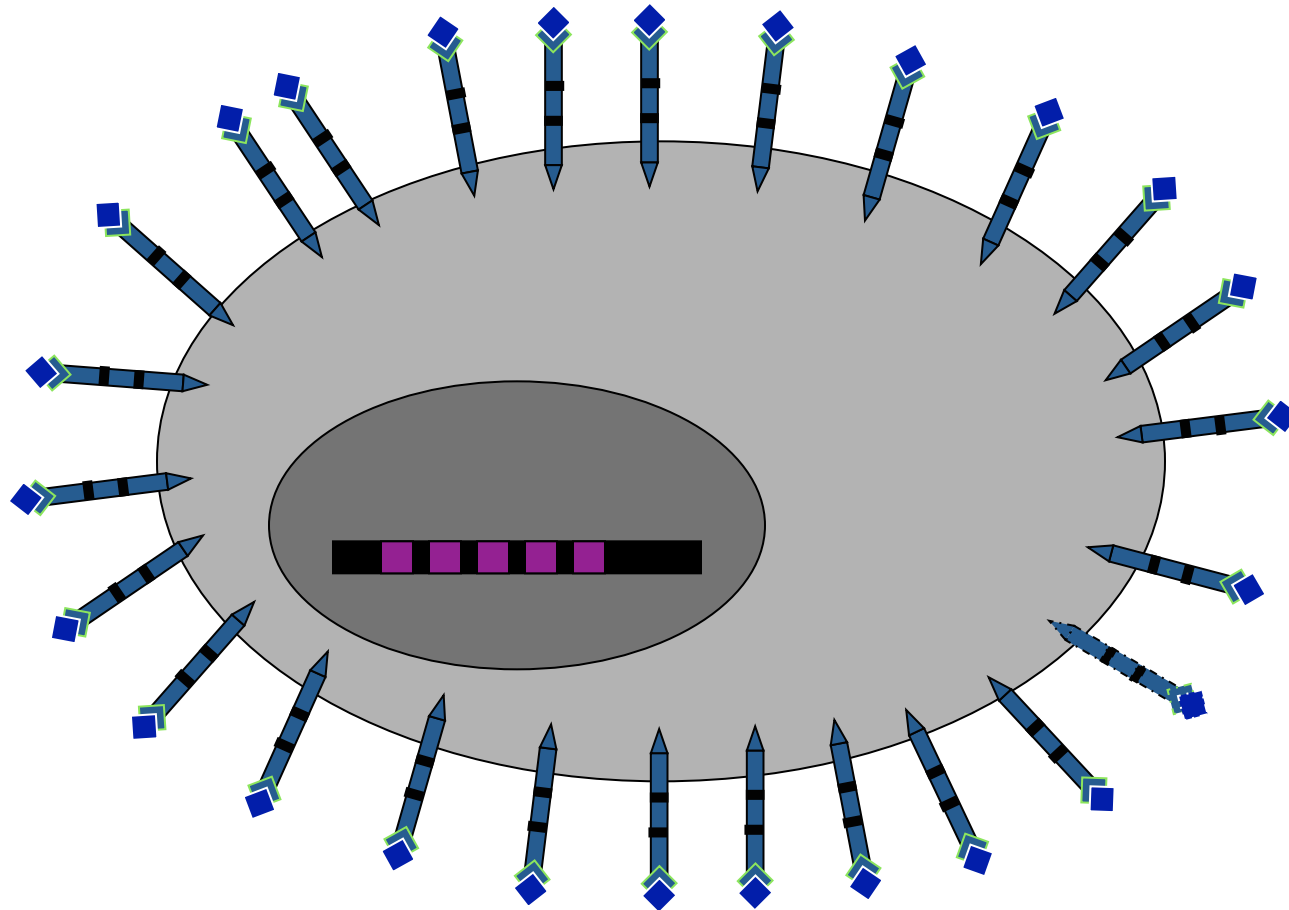
Too much
Protein

Breast Cancer

- Most common cancer in women.
- Ca. 1.000.000 will newly develop the disease per year.
- Ca. 400.000 die of the disease per year.
- 17.286 died in Germany in 2006 of breast cancer.

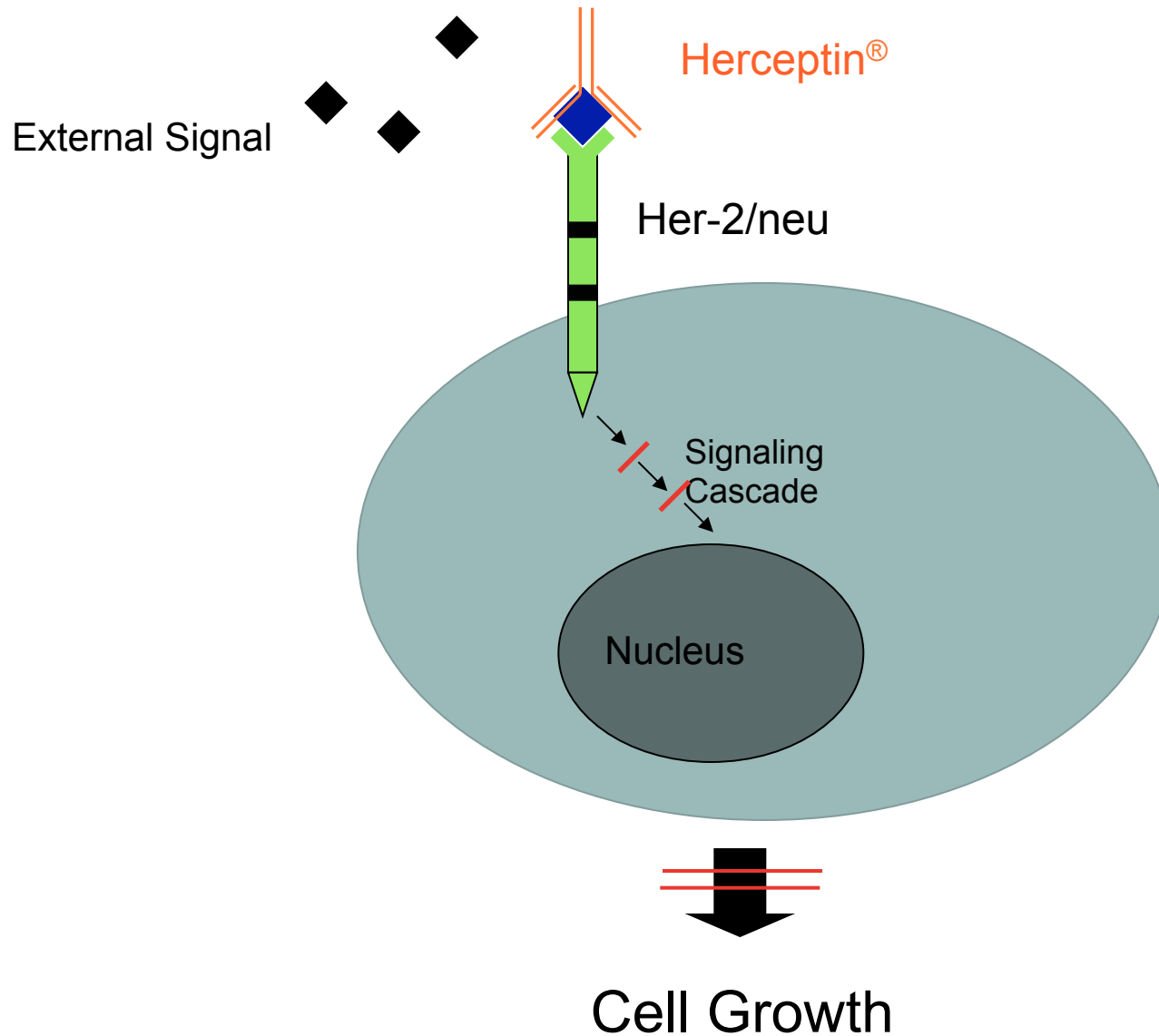


Her-2 Overexpression in Breast Cancer Cells

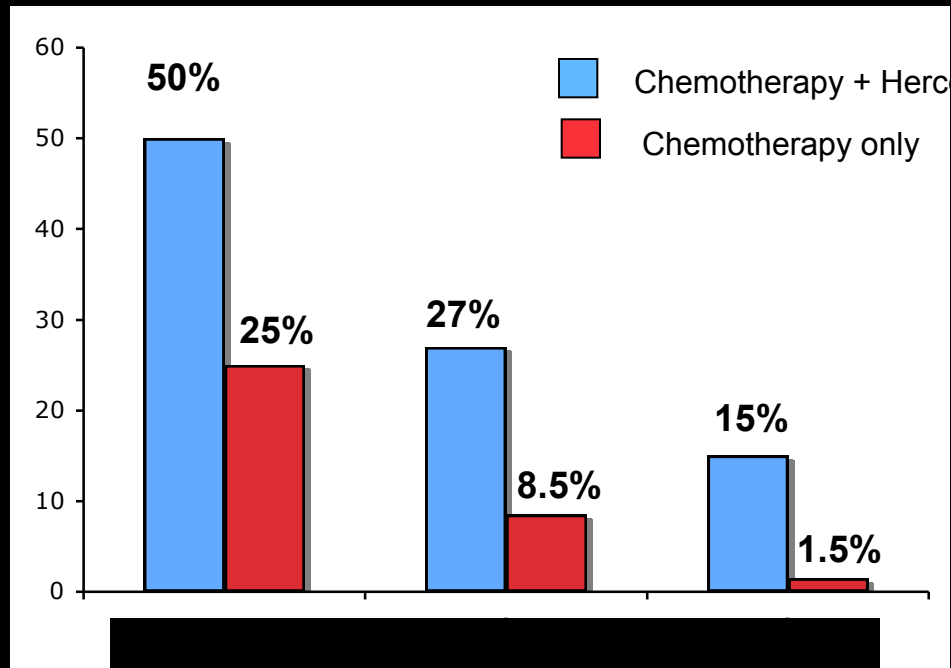


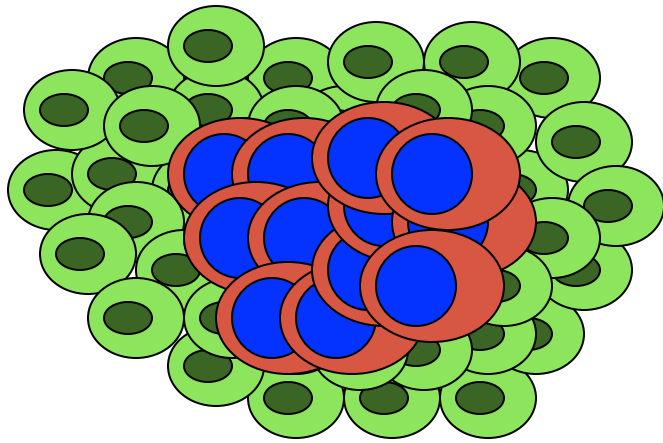
Deregulated Growth

Therapeutic Strategy: Monoclonal Antibodies



Progression Free Survival after Therapy with Herceptin®





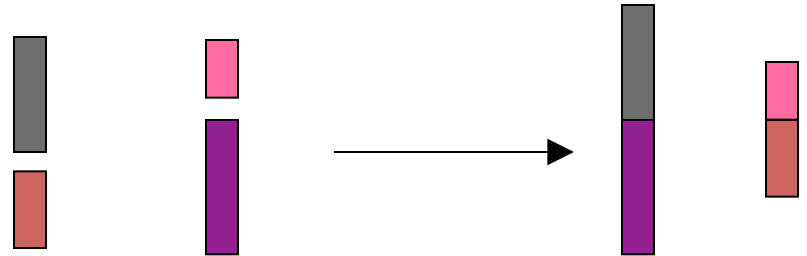
Tumor

DNA with Defect



Deregulated
Growth

Translocation



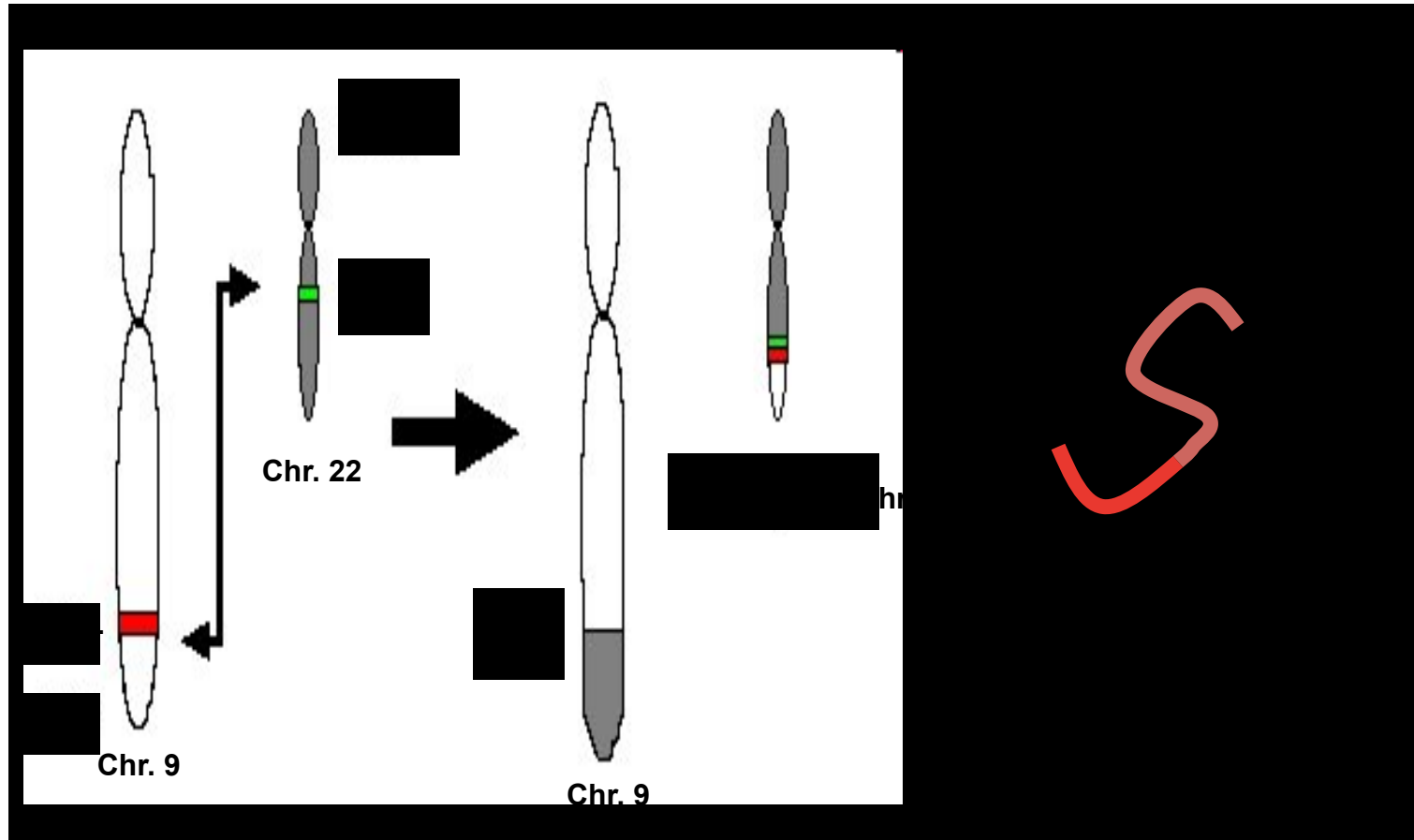
Generation of Fusion
Proteins

Chronic Myeloid Leukemia (CML)

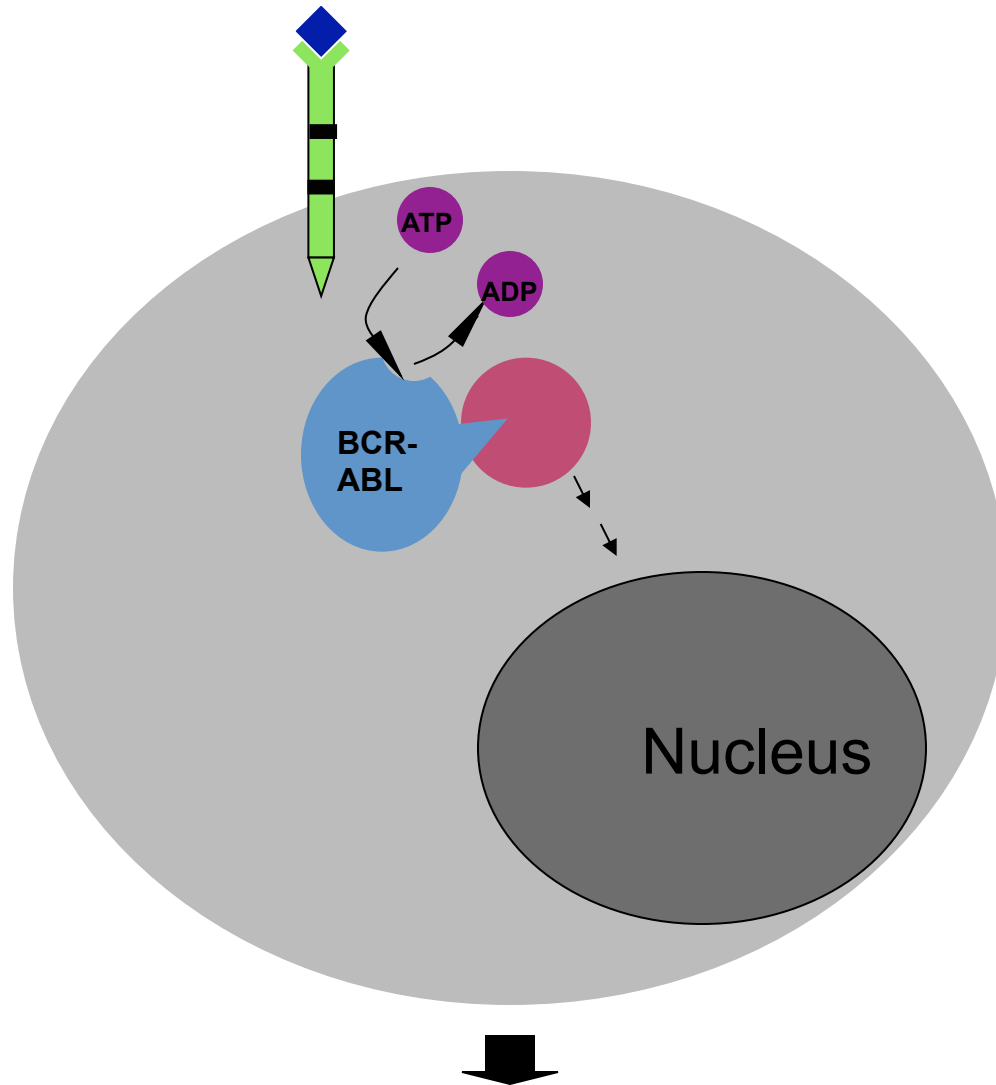
Philadelphia Chromosome



Biology of CML (Philadelphia Chromosome)

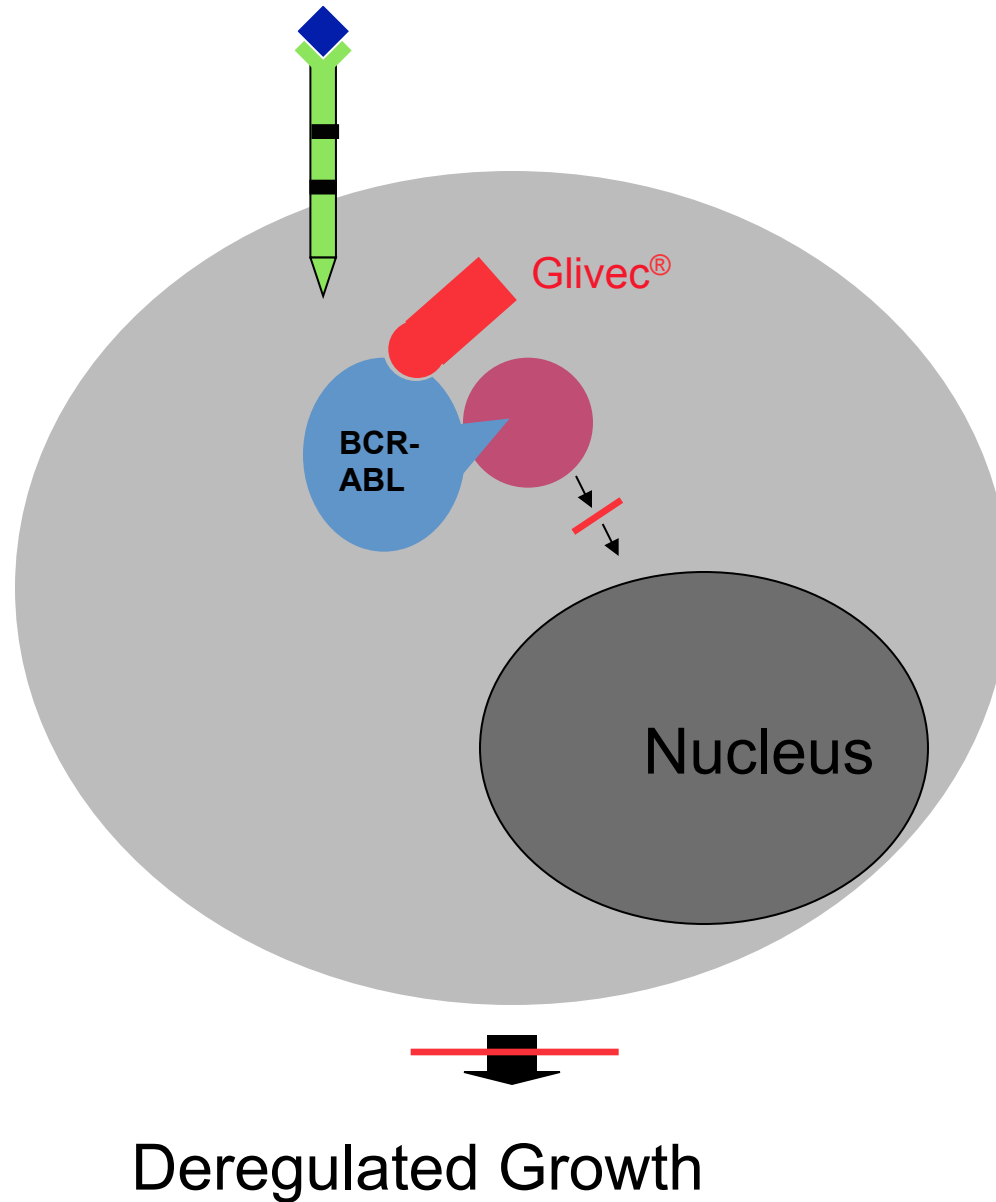


Chronic Myeloid Leukemia (CML)

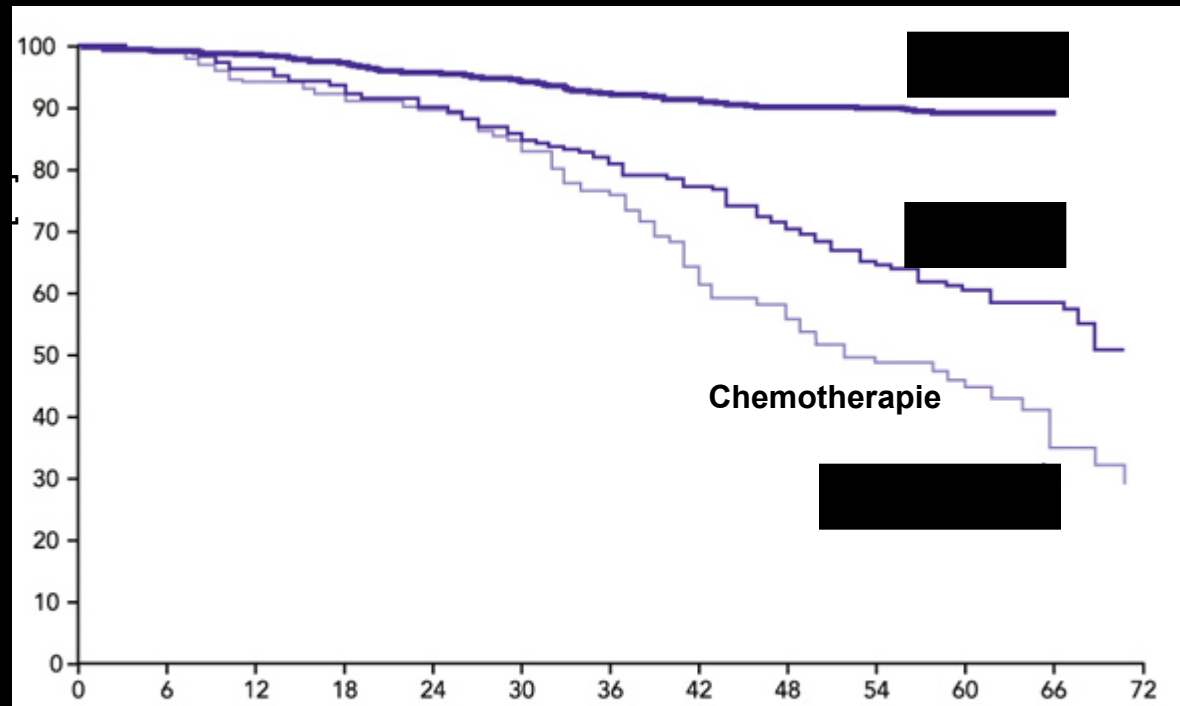


Deregulated Growth

Chronic Myeloid Leukemia (CML)



Overall Survival in CML



Further Mechanisms and Therapeutic Agents

VEGF (vascular endothelial growth factor)

- Avastin® (Bevacizumab)

Colon, Lung, Breast, Kidney, Brain

EGFR (epidermal growth factor receptor)

- Erbitux® (Cetuximab) Colon, Head/Neck
- Iressa® (Gefitinib) Lung

Life Expectancy and Health Expenditures

Table 1. Life Expectancy and Health Expenditures Worldwide³

Country	Life Expectancy (female-years)	Total Expense per Person (US \$)	% of GDP
Australia	83	2,519	9.5
Canada	83	2,669	9.9
Ireland	81	2,860	7.3
Japan	86	2,662	7.9
Monaco	85	4,587	9.7
Singapore	82	964	4.5
Spain	83	1,541	7.7
Switzerland	83	5,035	11.5
United Kingdom	81	2,428	8.0
United States	80	5,711	15.2

Abbreviation: GDP, gross domestic product.

Cost of Modern Cancer Therapeutics

Drug	Systematic name	Cancer Type	Costs/year
Avastin®	Bevacizumab	Colon, Lung, Breast	70.000 €
Iressa®	Gefitinib	Lung	40.000 €
Erbitux®	Cetuximab	Colon, Head/Neck	100.000 €
Glivec®	Imatinib	CML, GIST	40.000 €
Herceptin®	Trastuzumab	Breast, Gastric	120.000 €
Mabthera®	Rituximab	NHL	35.000 €
Tarceva®	Erlotinib	Lung, Pancreas	36.000 €
PLX4032	Vemurafenib	Malignant Melanom	100.000 €
Yervoy®	Ipilimumab	Malignant Melanom	140.000 €

Cost Efficiency of the Chemotherapeutic Treatment of Colon Cancer

1st Line	2nd Line	3rd Line	Life expectancy [weeks]	Total costs [U\$]
BSC	-	-	24.2	0
5-FU/FS	BSC	-	47.4	23.164
FOLFOX	BSC	-	65.2	78.815
FOLFOX	FOLFIRI	BSC	83.6	94.563
FOLFOX	FOLFIRI	Erbitux®	87.9	106.833
FOLFOX + Avastin®	FOLFIRI	BSC	99.8	165.649
FOLFIRI + Avastin®	FOLFOX	Erbitux®	105.2	165.360
FOLFOX + Avastin®	FOLFIRI	Erbitux®	105.2	175.964
FOLFIRI + Avastin®	FOLFOX	FOLFIRI + Erbitux®	112.9	191.773
FOLFOX + Avastin®	FOLFIRI	FOLFIRI + Erbitux®	113.7	205.384

Thank you for your attention!