



SHEET



SLIDE



Slide : 21-Tumor Immuniy



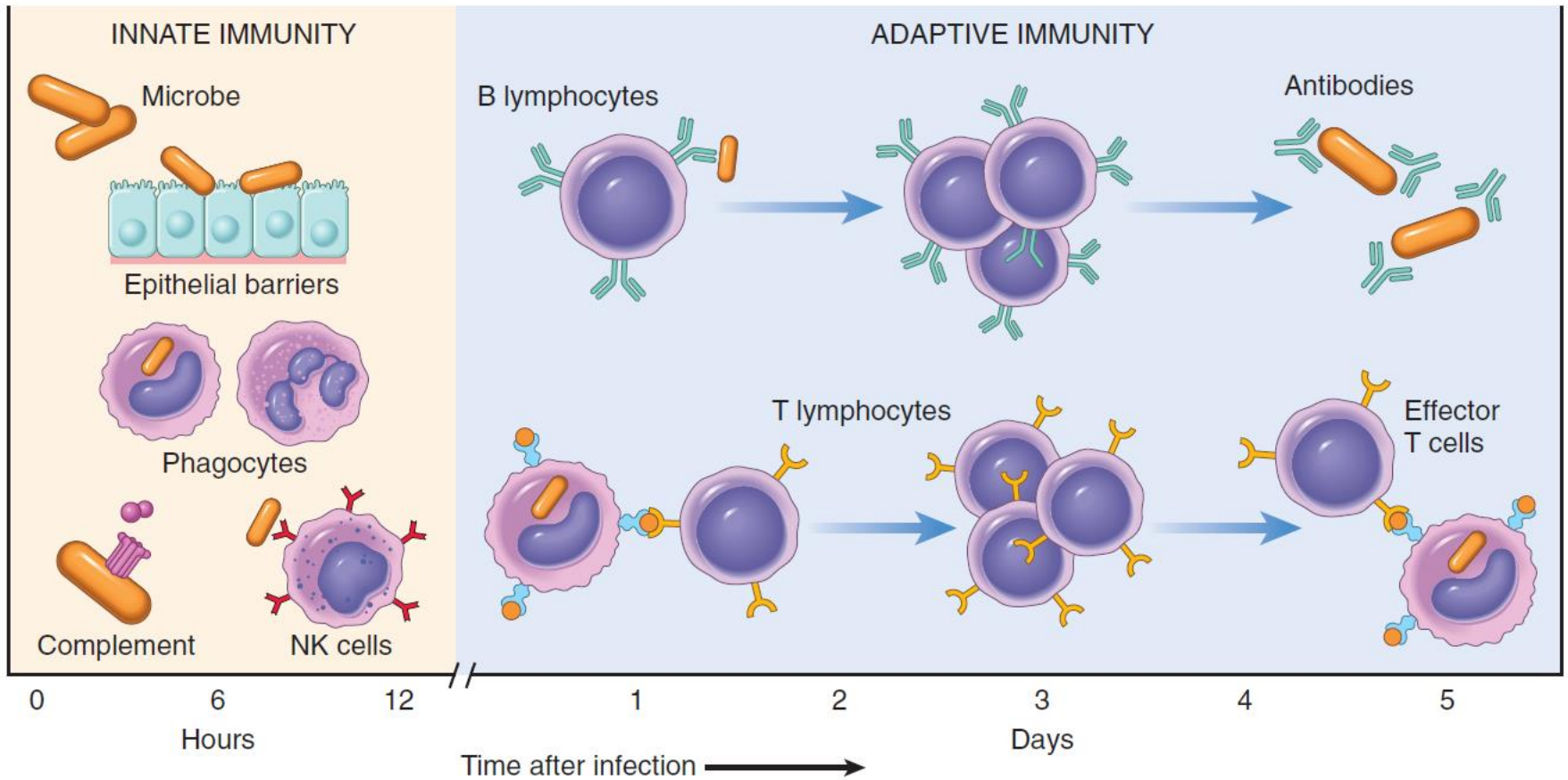
Doctor: Dr. Mazen





Tumor Immunity

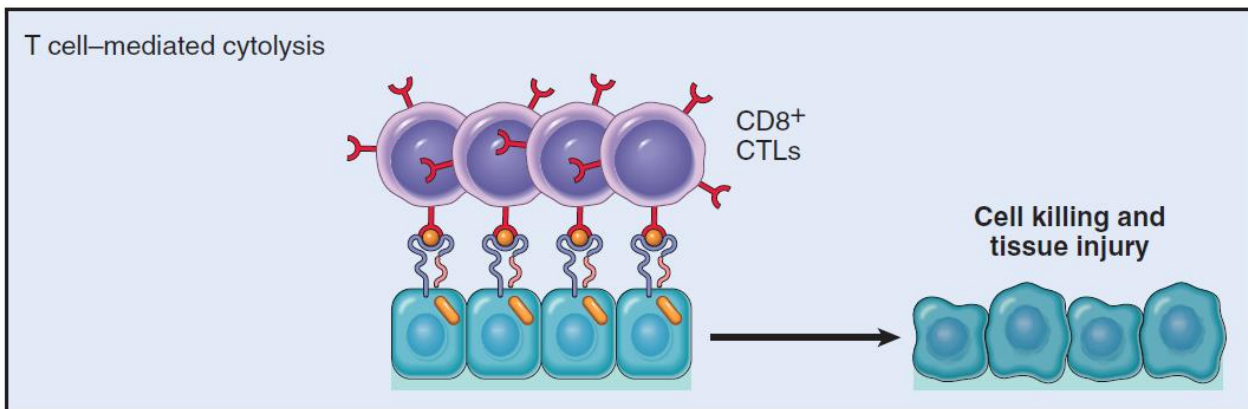
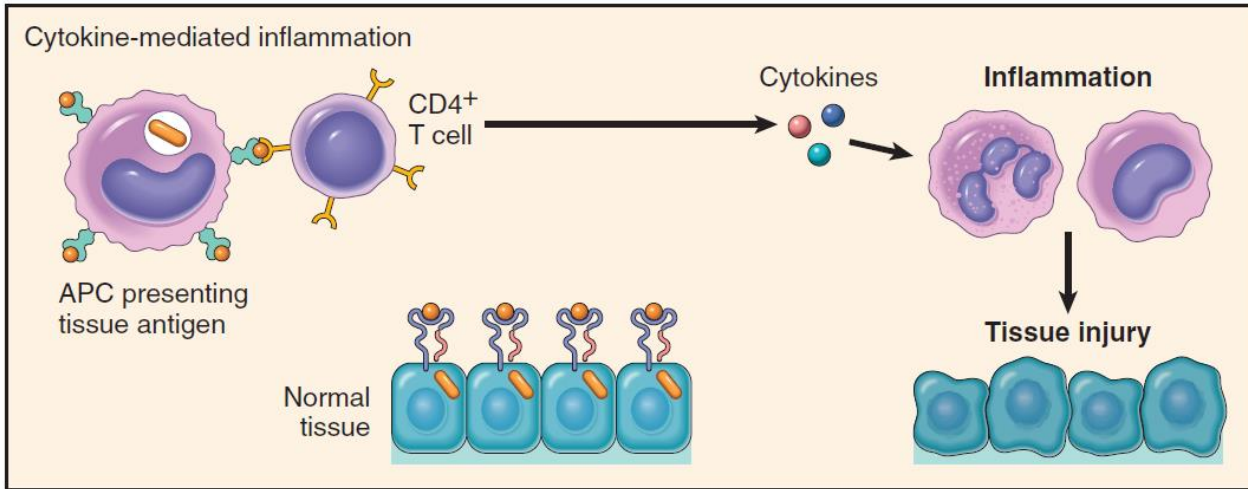
Innate/Adaptive-Humoral/Cell-mediated



CD4+/CD8+ T cells

CD4+ T cells: cytokine production

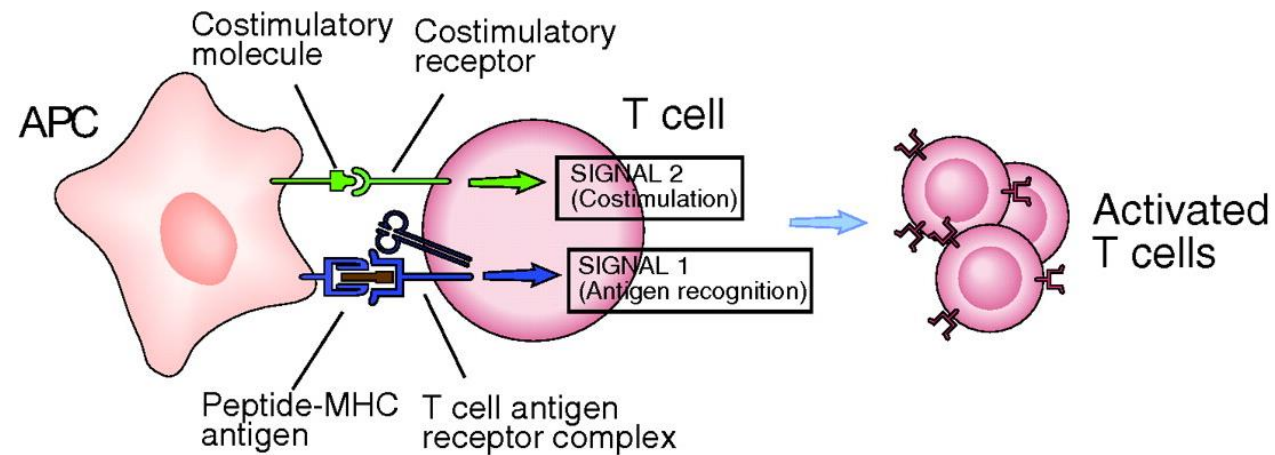
CD8+ T cells: direct killing

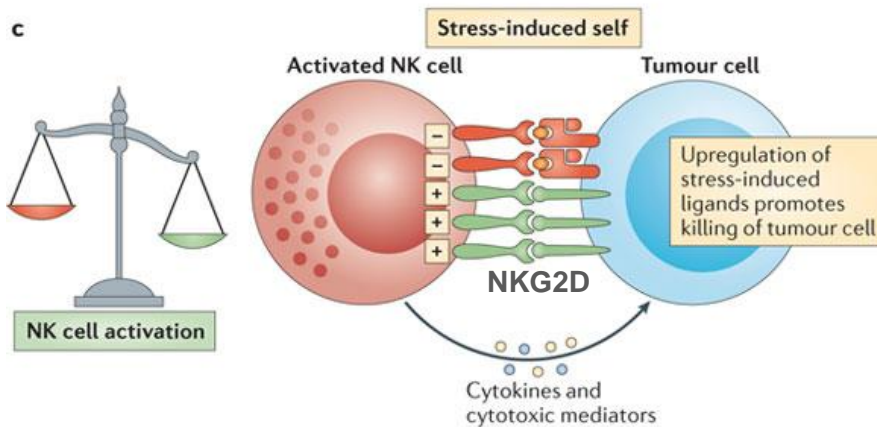
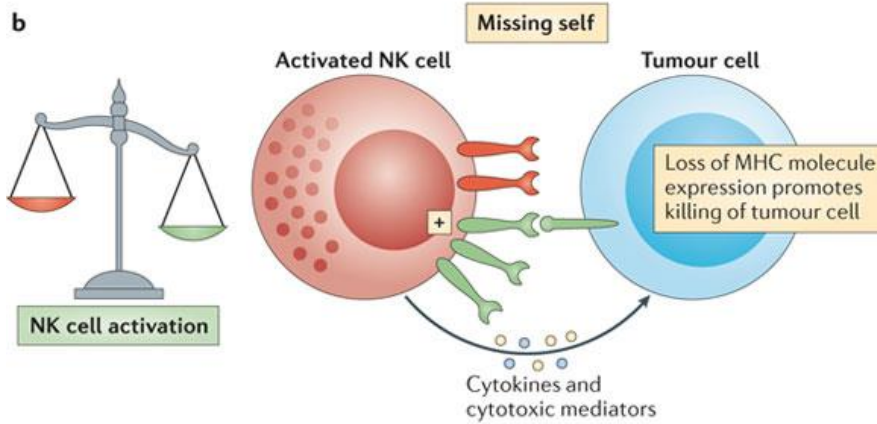
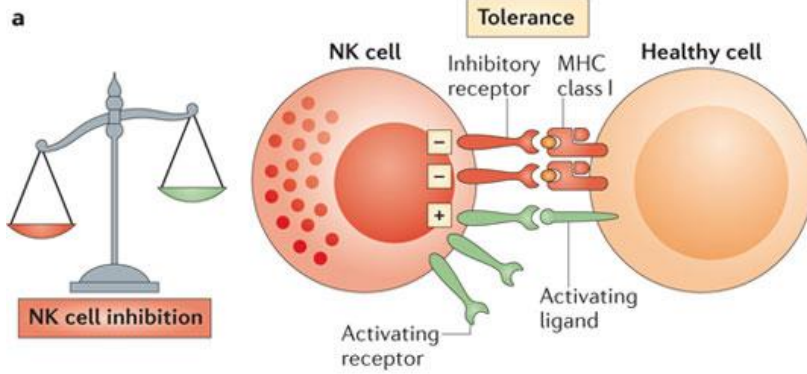


CD4+/CD8+ T cells

CD4+ T cells: cytokine production

CD8+ T cells: direct killing





NK cells

No Prior sensitization

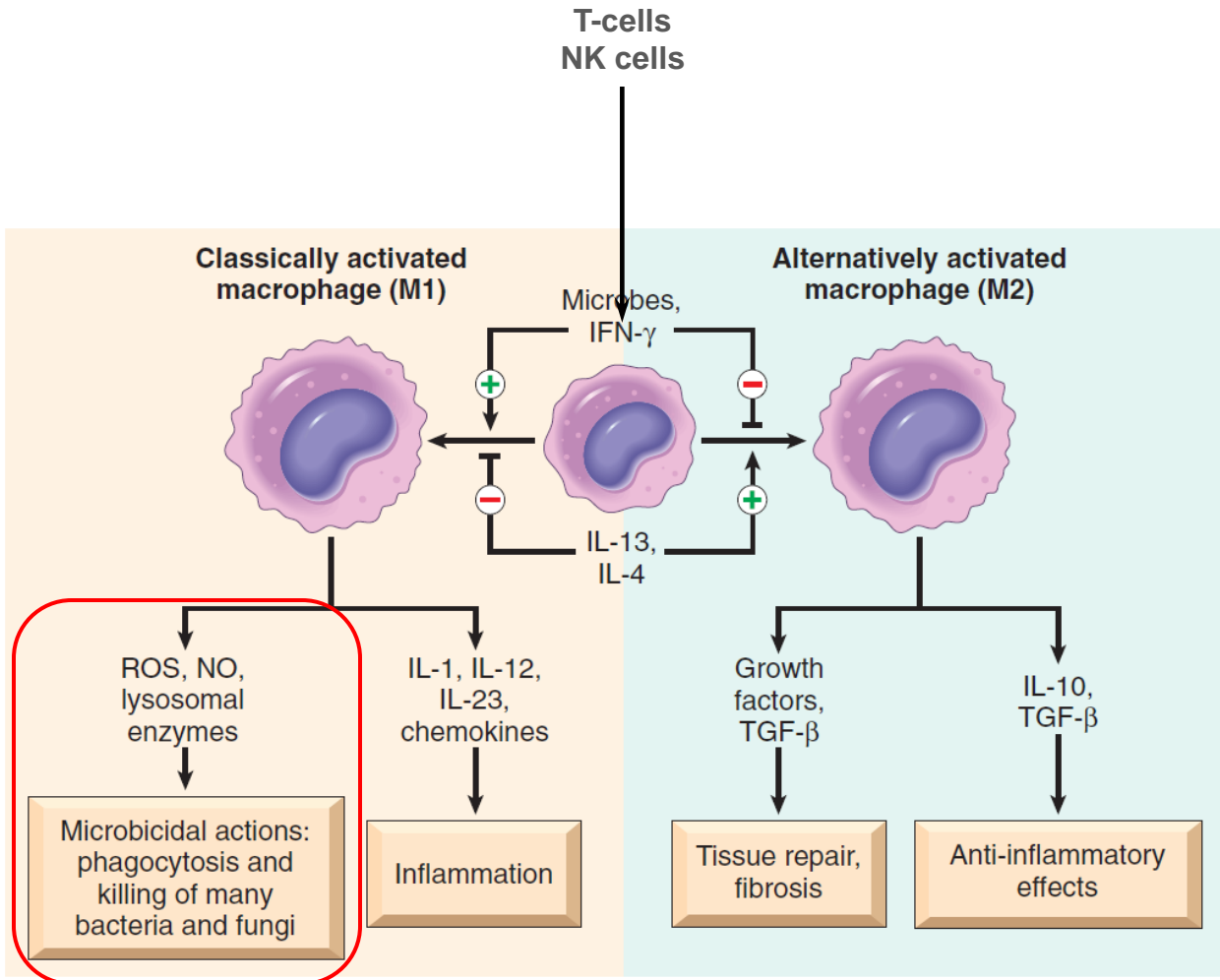
IL-2 induced activation

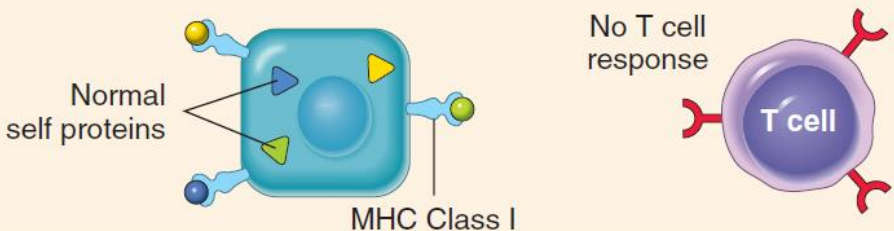
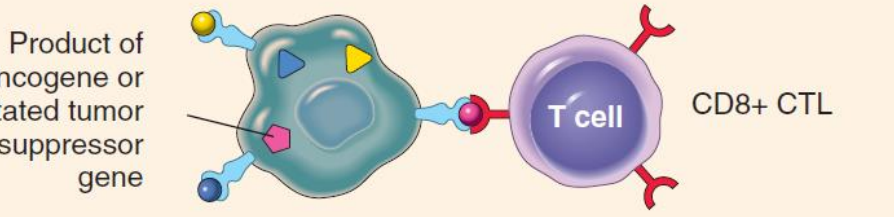
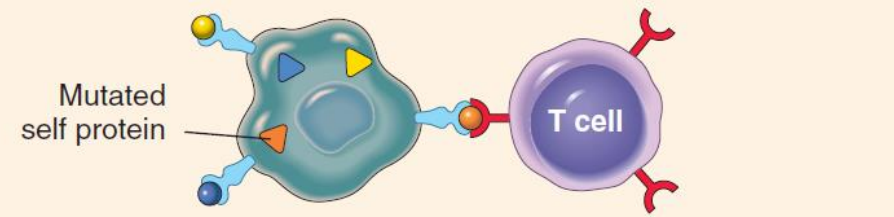
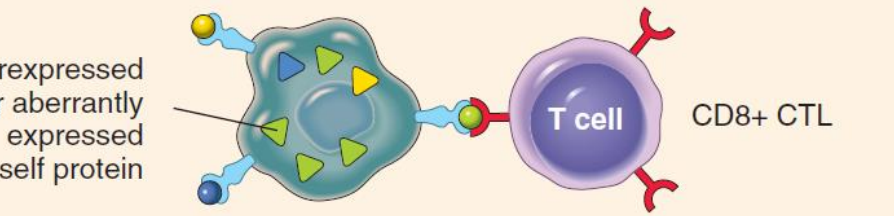
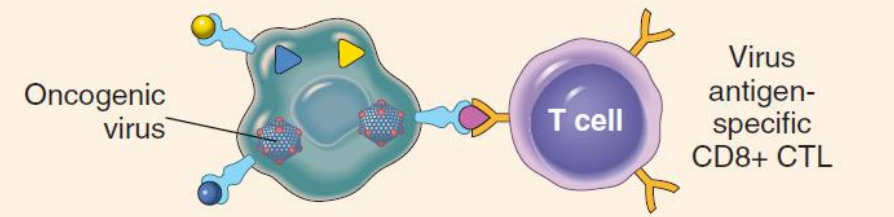
Stress induced ligands
(e.g. NKG2D ligands)
expressed:

- Tumor cells
- DNA damage

M1 macrophages

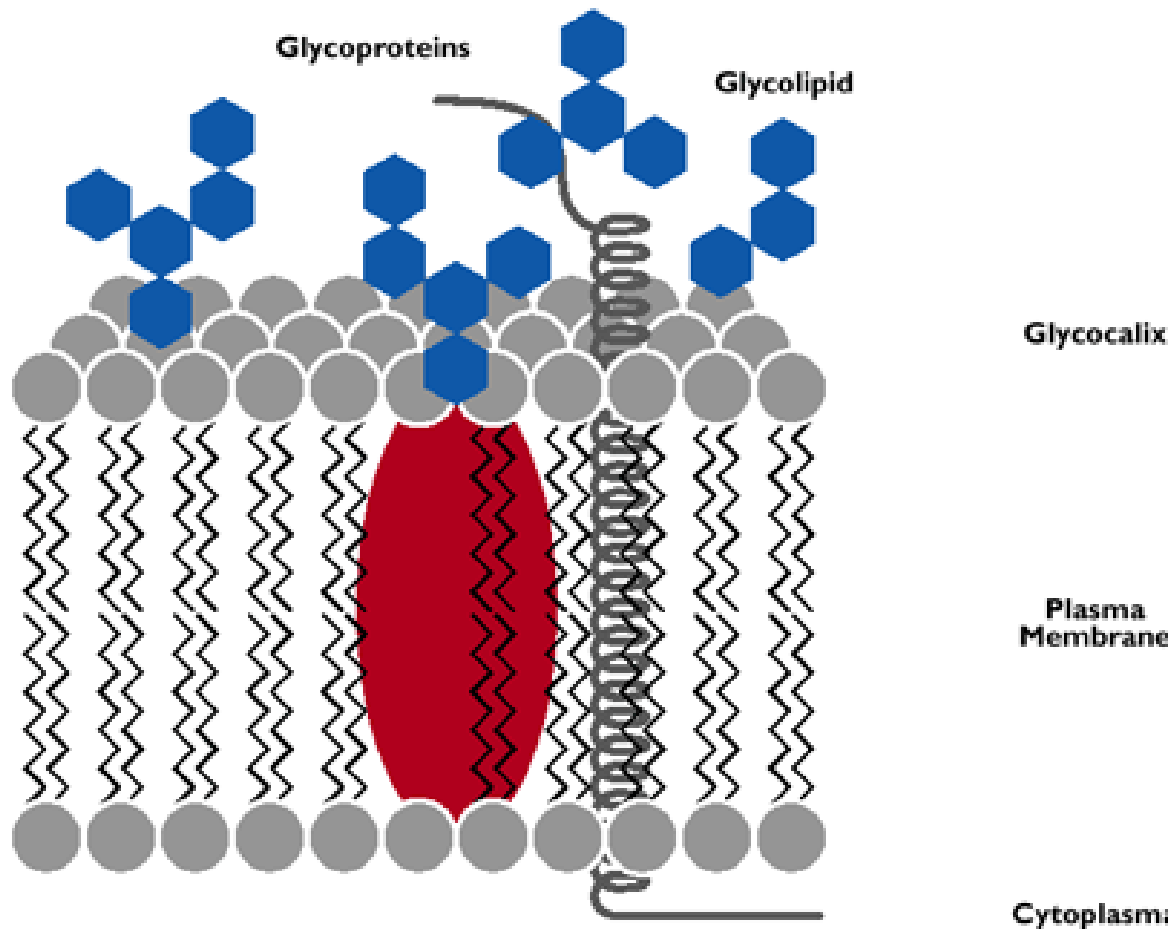
Kill tumor cells by similar mechanisms as used on microbes.



Normal host cell displaying multiple MHC-associated self antigens		EXAMPLES
Tumor cells expressing different types of tumor antigens		<p>Oncogene products: mutated RAS, BCR/ABL fusion proteins</p> <p>Tumor suppressor gene products: mutated p53 protein</p>
		<p>Various mutant proteins in carcinogen- or radiation-induced animal tumors; various mutated proteins in melanomas</p>
		<p>Overexpressed: tyrosinase, gp100, MART in melanomas Oncofetal antigens (CEA) Aberrantly expressed: cancer-testis antigens (MAGE, BAGE) Differentiation antigens (CD20)</p>
		<p>Human papilloma virus E6, E7 proteins in cervical carcinoma; EBNA proteins in EBV-induced lymphoma</p>



Glycolipids and Glycoproteins



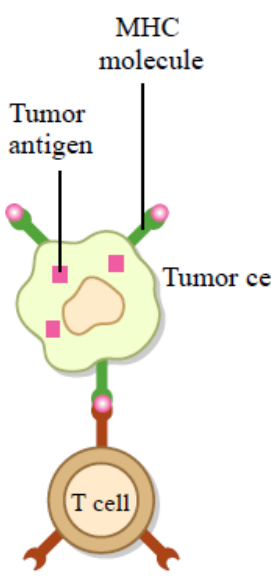
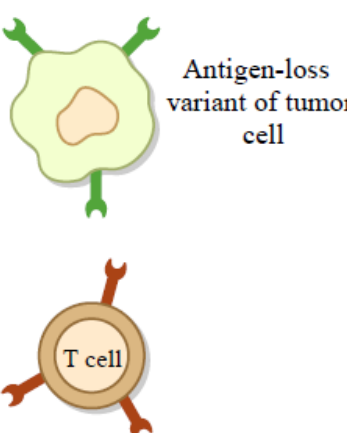
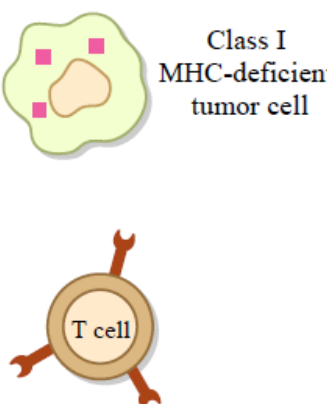
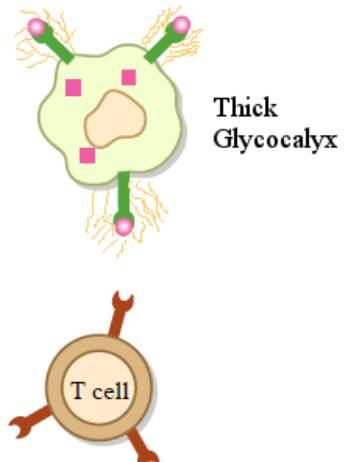
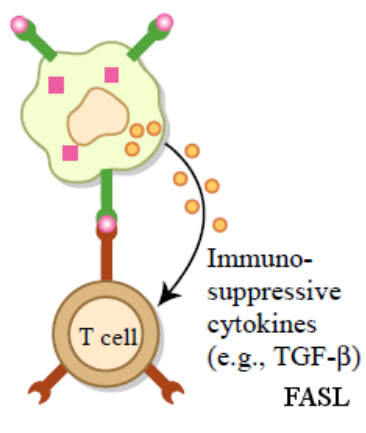
Increased/abnormal

CA-125/CA-19-9 Ovarian carcinomas

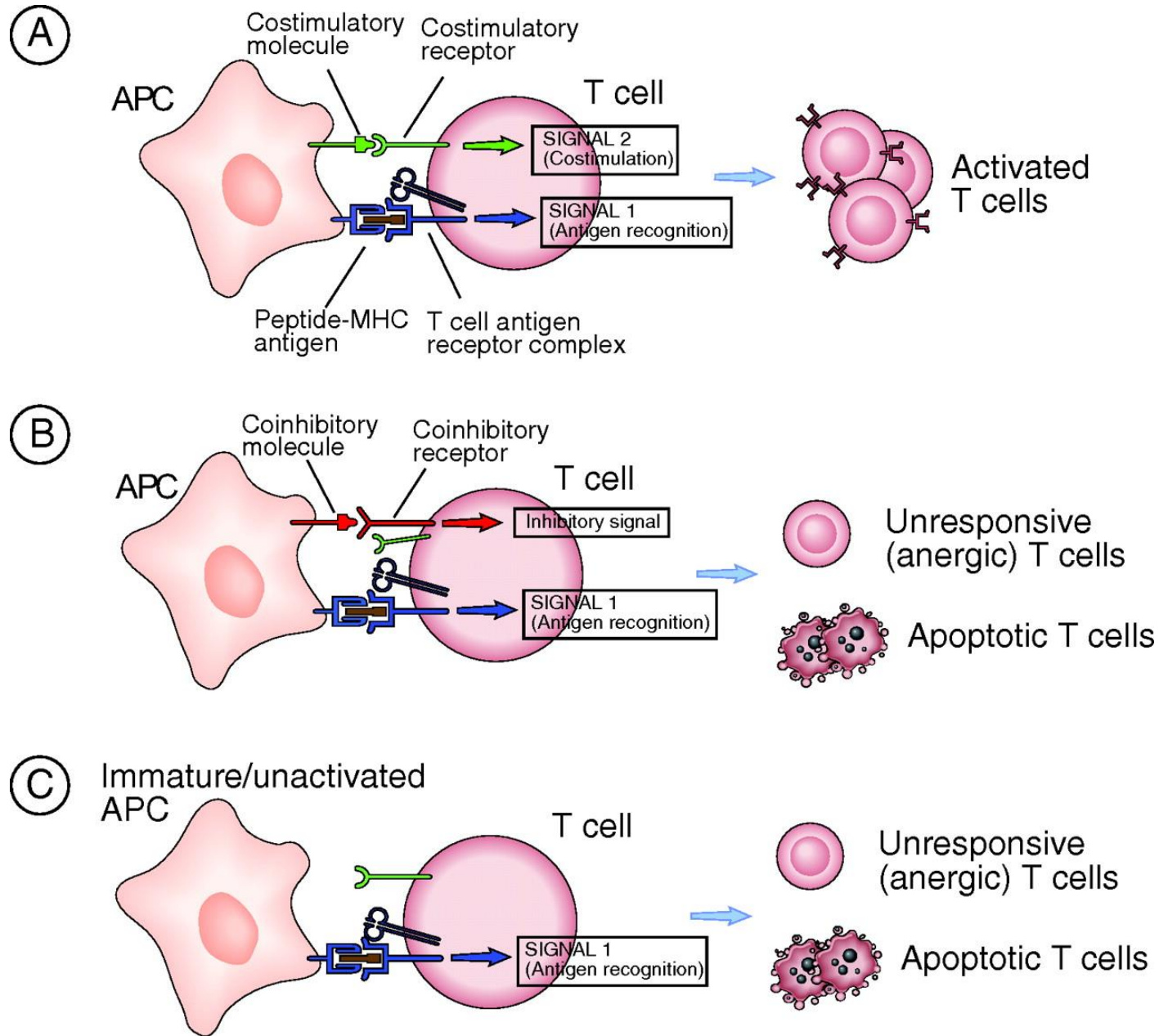
MUC-1 Breast carcinomas

Diagnostic/therapeutic targets



Anti-tumor immunity	Immune evasion by tumors			
 <p>MHC molecule</p> <p>Tumor antigen</p> <p>Tumor cell</p> <p>T cell</p> <p>T cell specific for tumor antigen</p>	<p>Failure to produce tumor antigen</p>  <p>Antigen-loss variant of tumor cell</p> <p>T cell</p>	<p>Mutations in MHC genes or genes needed for antigen processing</p>  <p>Class I MHC-deficient tumor cell</p> <p>T cell</p>	<p>Antigen masking</p>  <p>Thick Glycocalyx</p> <p>T cell</p>	<p>Production of immuno-suppressive protein</p>  <p>Immuno-suppressive cytokines (e.g., TGF-β) FASL</p> <p>T cell</p>
T cell recognition of tumor antigen leading to T cell activation	Lack of T cell recognition of tumor	Lack of T cell recognition of tumor	Lack of T cell recognition of tumor	Inhibition of T cell activation

Downregulation of co-stimulatory molecules

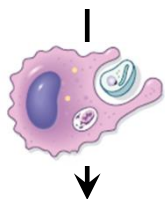
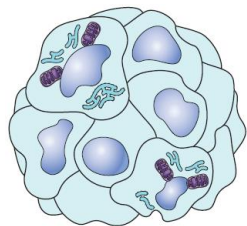


Clinical Aspects of Neoplasia

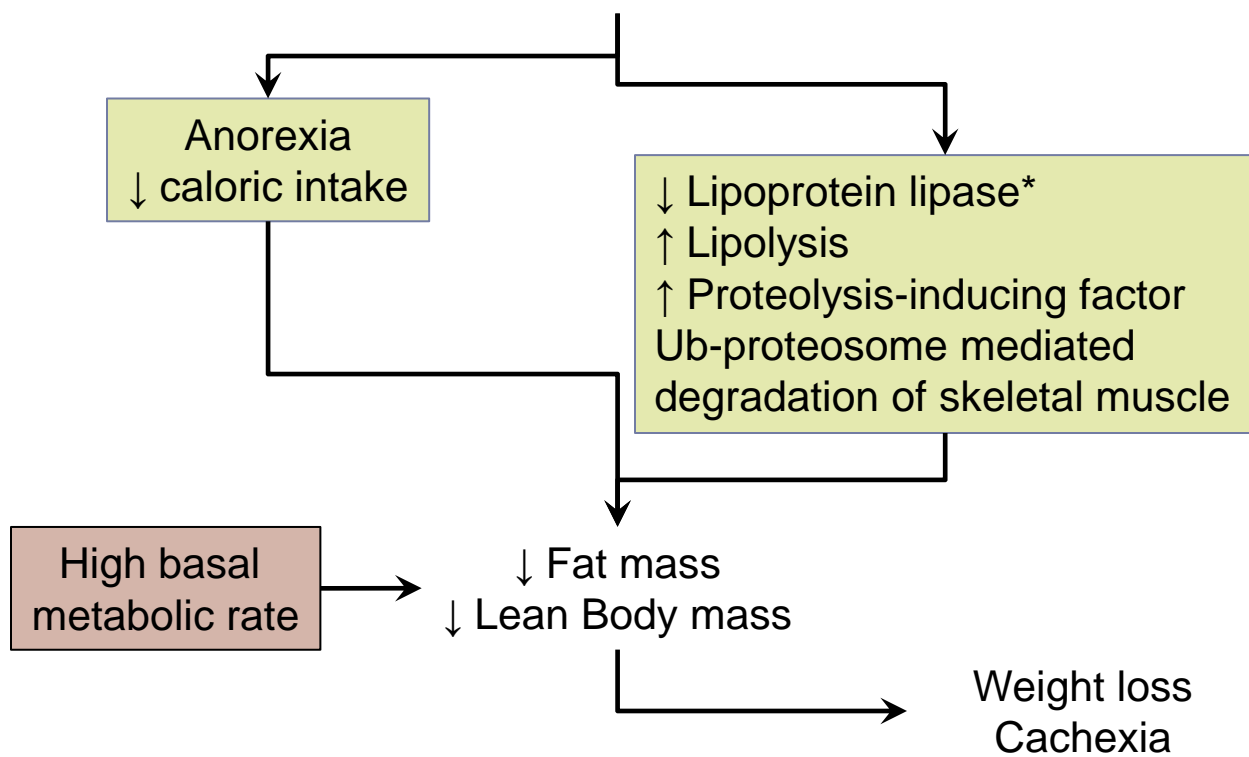
Tumor effects on host QUIZ

- ▶ Location
- ▶ Function
- ▶ Ulceration/bleeding/infection/rupture/infarction
- ▶ Cachexia





TNF



Cancer Cachexia

Correlation between size/spread and cachexia severity

Cachexia is **not** caused by tumor nutritional demands



Paraneoplastic syndromes

Not explained by primary tumor or metastasis

Hormones produced are not indigenous to the diseased tissue

Important in:

- Diagnosis
- Pathology
- Treatment strategy

Clinical Syndrome	Major Forms of Neoplasia	Causal Mechanism(s)/Agent(s)
Endocrinopathies		
Cushing syndrome	Small cell carcinoma of lung Pancreatic carcinoma Neural tumors	ACTH or ACTH-like substance
Syndrome of inappropriate antidiuretic hormone secretion	Small cell carcinoma of lung; intracranial neoplasms	Antidiuretic hormone or atrial natriuretic hormones
Hypercalcemia	Squamous cell carcinoma of lung Breast carcinoma Renal carcinoma Adult T cell leukemia/lymphoma Ovarian carcinoma	Parathyroid hormone-related protein, TGF- α , TNF, IL-1
Hypoglycemia	Fibrosarcoma Other mesenchymal sarcomas Hepatocellular carcinoma	Insulin or insulin-like substance
Carcinoid syndrome	Bronchial adenoma (carcinoid) Pancreatic carcinoma Gastric carcinoma	Serotonin, bradykinin
Polycythemia	Renal carcinoma Cerebellar hemangioma Hepatocellular carcinoma	Erythropoietin
Nerve and Muscle Syndrome		
Myasthenia	Bronchogenic carcinoma, thymoma	Immunologic
Disorders of the central and peripheral nervous systems	Breast carcinoma, teratoma	
Dermatologic Disorders		
Acanthosis nigricans	Gastric carcinoma Lung carcinoma Uterine carcinoma	Immunologic; secretion of epidermal growth factor
Dermatomyositis	Bronchogenic and breast carcinoma	Immunologic
Osseous, Articular, and Soft Tissue Changes		
Hypertrophic osteoarthropathy and clubbing of the fingers	Bronchogenic carcinoma	Unknown
Vascular and Hematologic Changes		
Venous thrombosis (Trousseau phenomenon)	Pancreatic carcinoma Bronchogenic carcinoma Other cancers	Tumor products (mucins that activate clotting)
Nonbacterial thrombotic endocarditis	Advanced cancers	Hypercoagulability
Anemia	Thymoma	Immunologic
Others		
Nephrotic syndrome	Various cancers	Tumor antigens, immune complexes



Grading & Staging

- ▶ Based on differentiation

- ▶ Cytological

- ▶ I-IV

- ▶ Varies with cancer type

- ▶ Based on size & spread

- ▶ Clinical/radiographic/surgical assessment

- ▶ TNM: Tumor T1-T4
 Node N0-N3
 Metastasis M0-M1

- ▶ AJC combines all of the above into stages I-IV



Grading & Staging (colorectal cancer)

Designation	Description
Tumor	
Tis	In situ dysplasia or intramucosal carcinoma
T1	Tumor invades submucosa
T2	Tumor invades into, but not through, muscularis propria
T3	Tumor invades through muscularis propria
T4	Tumor invades adjacent organs or visceral peritoneum
Regional Lymph Nodes	
NX	Lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in one to three regional lymph nodes
N2	Metastasis in four or more regional lymph nodes
Distant Metastasis	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis or seeding of abdominal organs

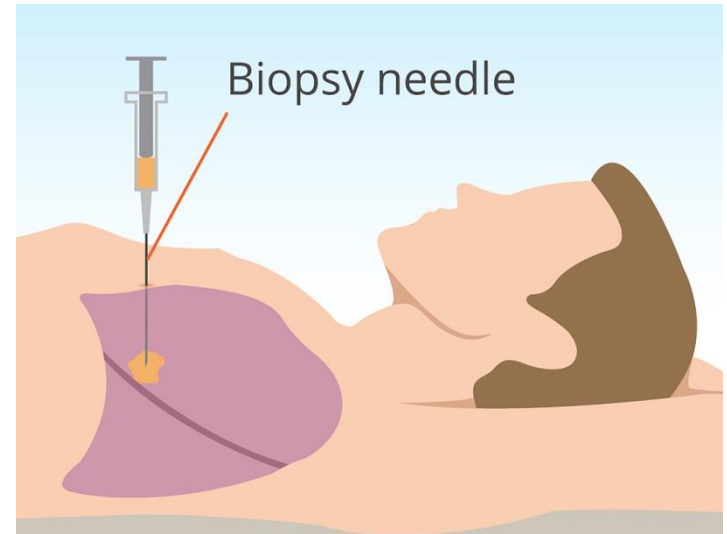
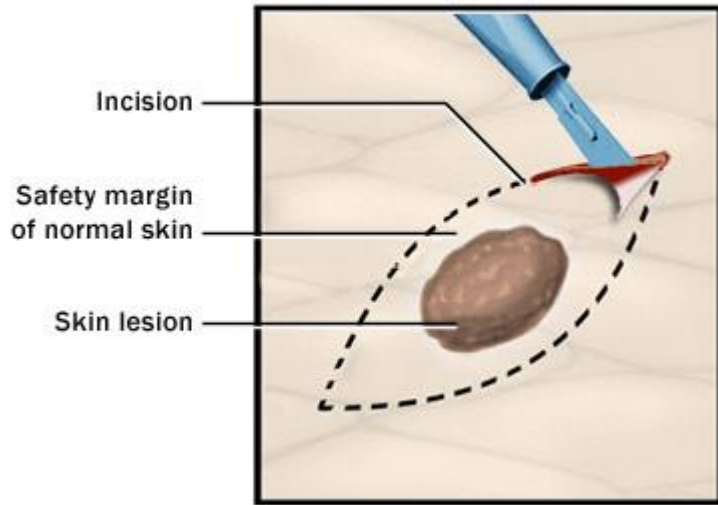
Stage*	Tumor-Node-Metastasis (TNM) Criteria			5-Year Survival (%)
	T	N	M	
I	T1, T2	N0	M0	74
II	IIA	T3	N0	67
	IIB	T4	N0	59
III	IIIA	T1, T2	N1	73
	IIIB	T3, T4	N1	46
	IIIC	Any T	N2	28
IV	Any T	Any N	M1	6





Lab diagnosis

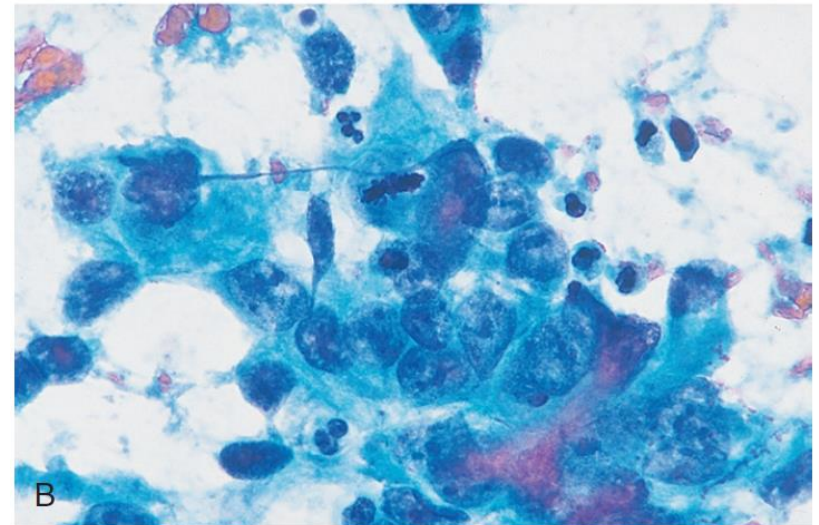
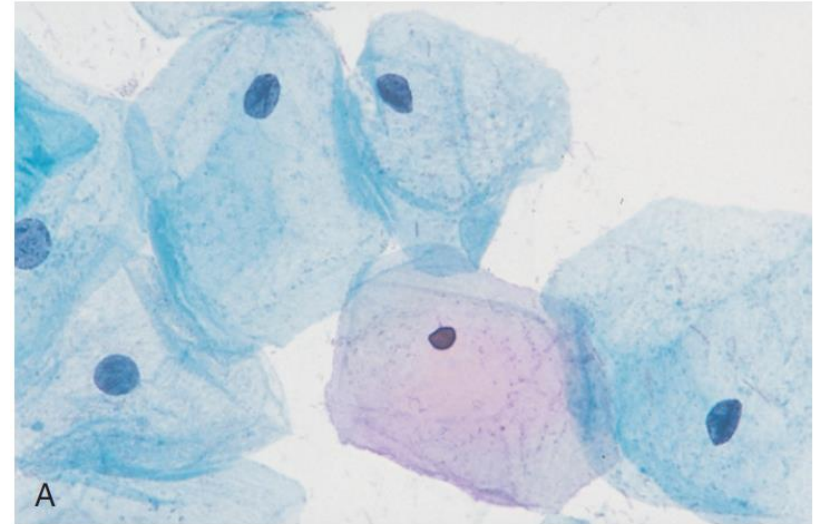
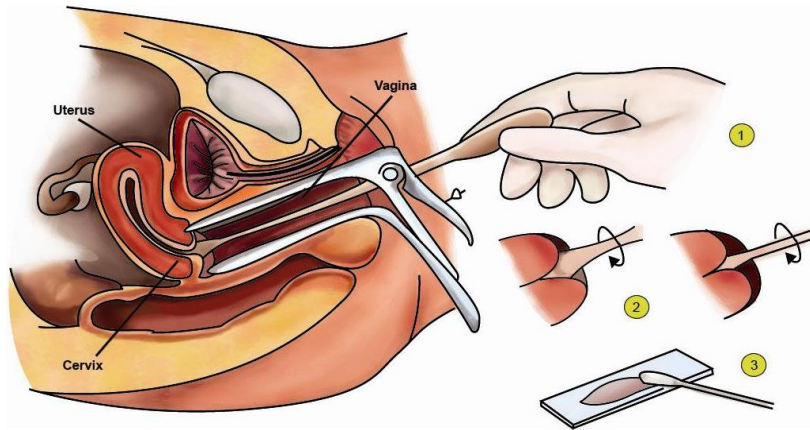
Biopsies



Excisional vs selective

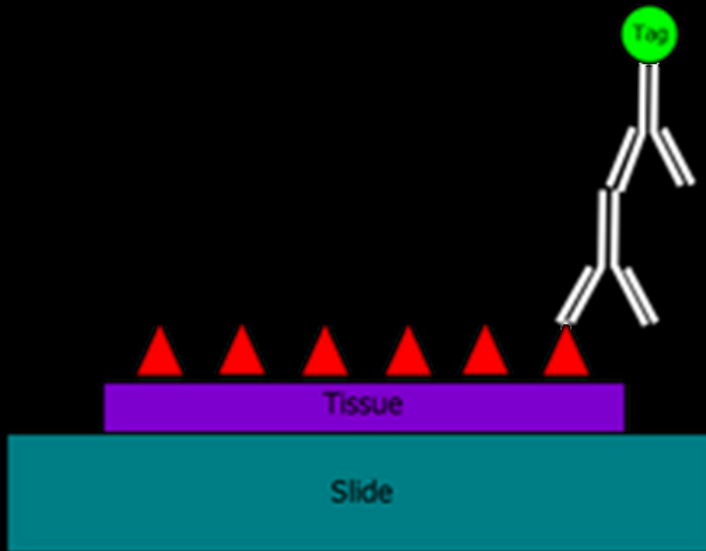


Biopsies

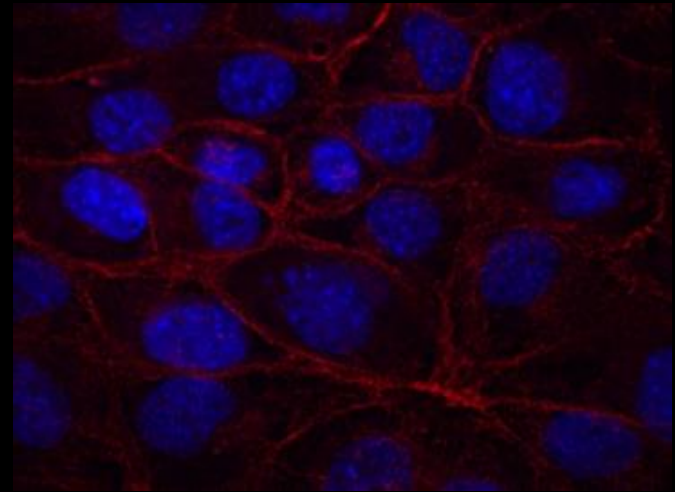


Neoplastic cells are less cohesive than other cells

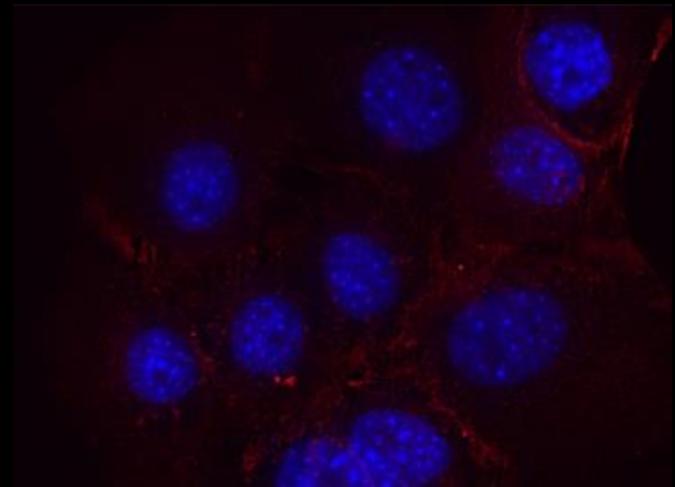
Immunocytochemistry/Immunohistochemistry



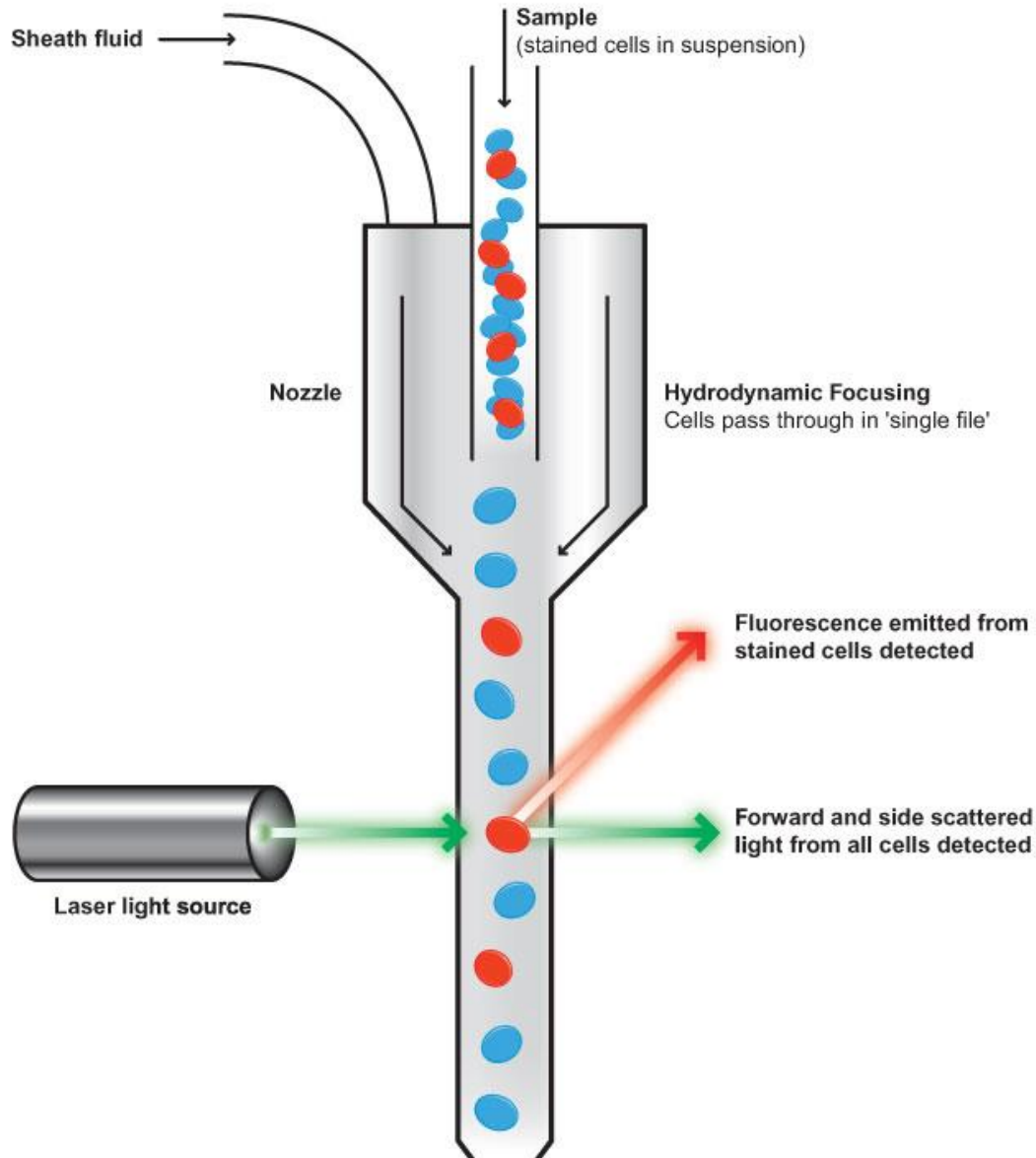
Control



TGF β



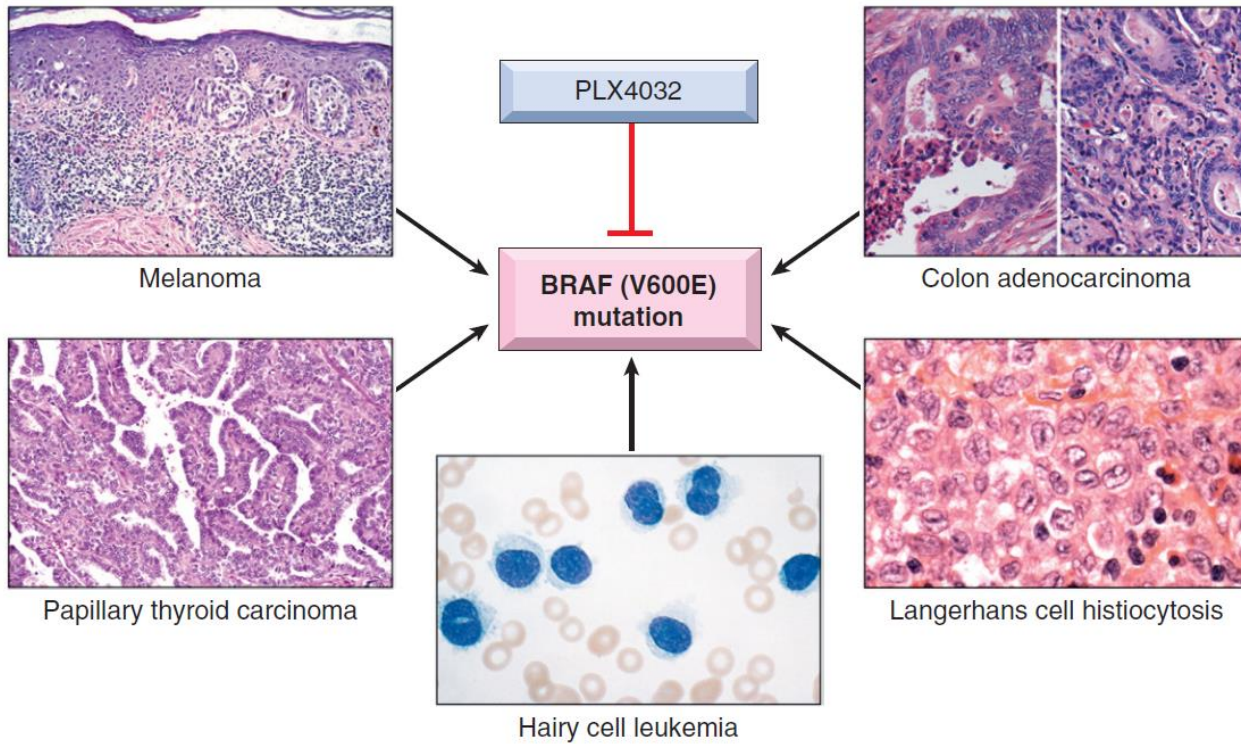
Flow Cytometry



Flow cytometry

Classification of
leukemias and
lymphomas

Molecular Techniques



Diagnosis

Genetic testing

Prognosis

Treatment decisions

Response

