Lymphoma Overview

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Overview

- ❑ What is lymphoma?
- ❑ How common is lymphoma?
- ❑ Who gets lymphoma?
- ❑ What is the general approach to a lymphoma patient?
- ❑ What general kinds of treatment are available?

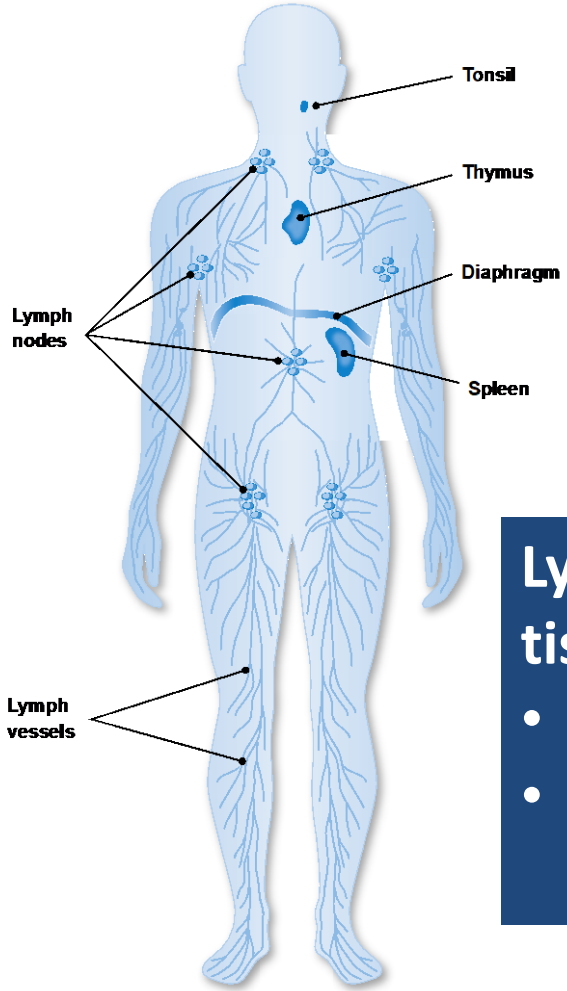
What is lymphoma?

Lymphoma is a family of blood cancers that comes from cancerous lymphocytes

B-cells **T-cells** **NK-cells**

- Lymphocytes normally fight viruses, bacteria, fungi, and foreign organisms
- Lymphocytes travel in lymphatic system
- These cells can grow in lymph nodes (nodal sites) or outside the lymph nodes (extranodal sites)

The Lymphatic System: where the cells of the immune system work and travel



- We have a lot of "lymphoid tissue" in our bodies
- Lymph nodes are normal
- Lymph nodes normally enlarge and become painful with infection

Lymphoma often grows in lymphoid tissues

- "nodal"= growing in a lymph node
- "extranodal"=growing outside of a lymph node

How Common is Lymphoma?

Estimated New Cases

Male		
Prostate	174,650	20%
Lung & bronchus	116,440	13%
Colon & rectum	78,500	9%
Urinary bladder	61,700	7%
Melanoma of the skin	57,220	7%
Kidney & renal pelvis	44,120	5%
Non-Hodgkin lymphoma	41,090	5%
Oral cavity & pharynx	38,140	4%
Leukemia	35,920	4%
Pancreas	29,940	3%
All sites	870,970	

Female		
Breast	268,600	30%
Lung & bronchus	111,710	13%
Colon & rectum	67,100	7%
Uterine corpus	61,880	7%
Melanoma of the skin	39,260	5%
Thyroid	37,810	4%
Non-Hodgkin lymphoma	33,110	4%
Kidney & renal pelvis	29,700	3%
Pancreas	26,830	3%
Leukemia	25,860	3%
All sites	891,480	

~74,000 new cases/year

662,789 people living with lymphoma

Hodgkin and non-Hodgkin lymphoma affect both genders, all ages, all races

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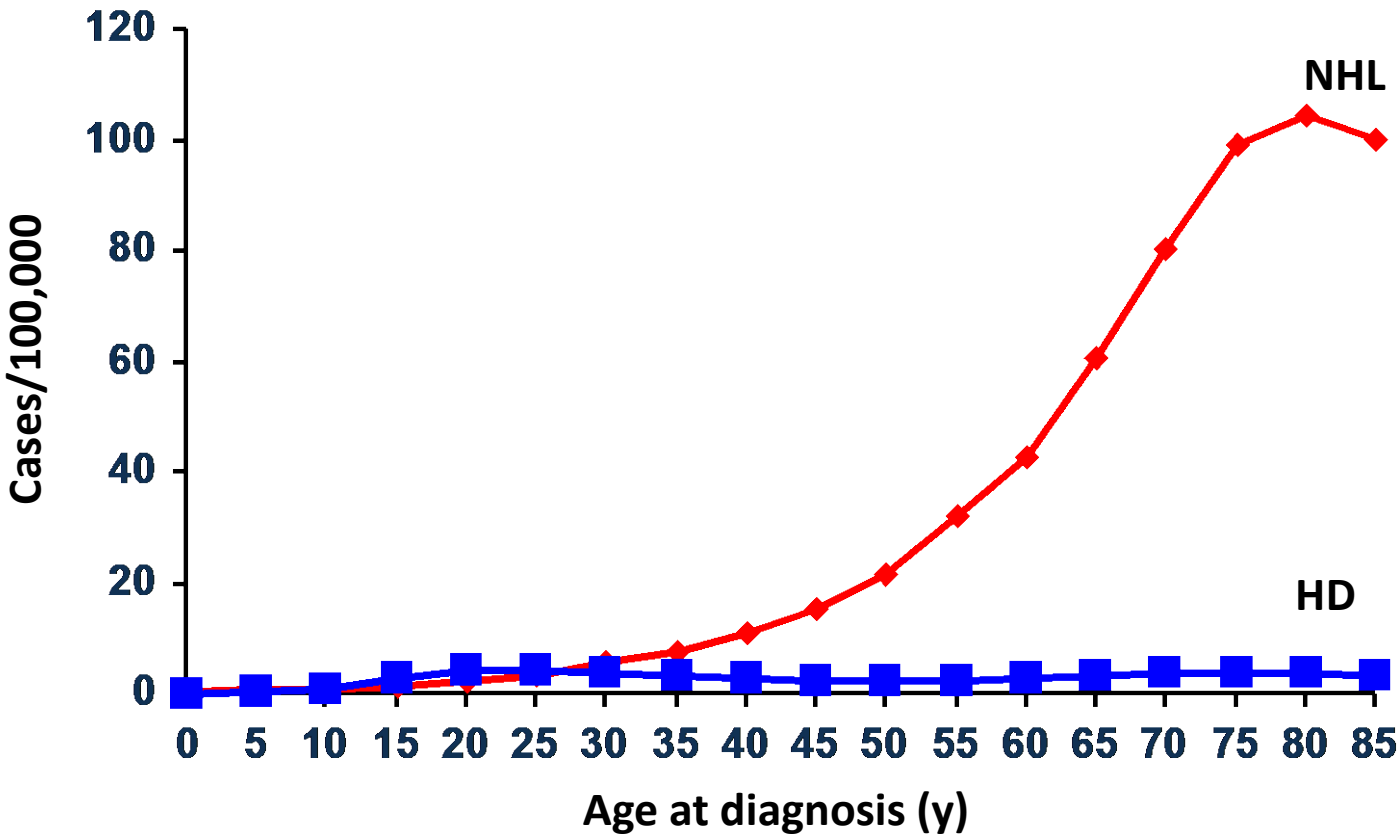
American Cancer Society. *Cancer Facts & Figures 2019*. Atlanta, GA: American Cancer Society; 2019.

Age at Diagnosis for Hodgkin and Non-Hodgkin Lymphoma



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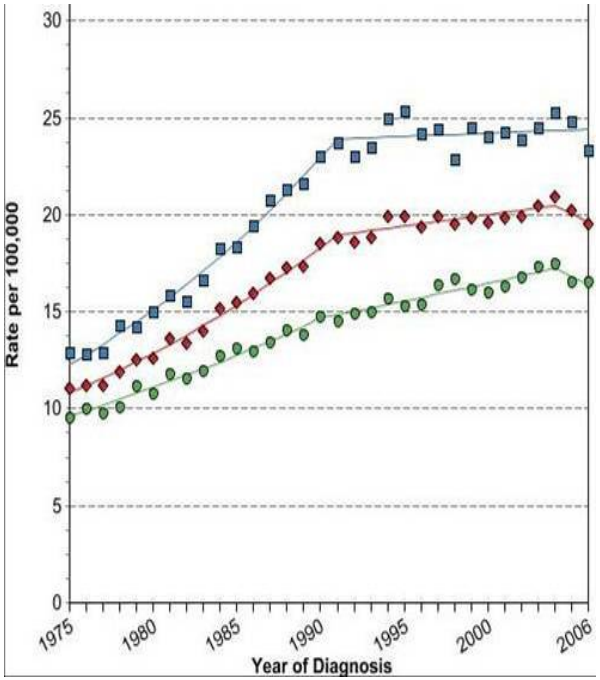
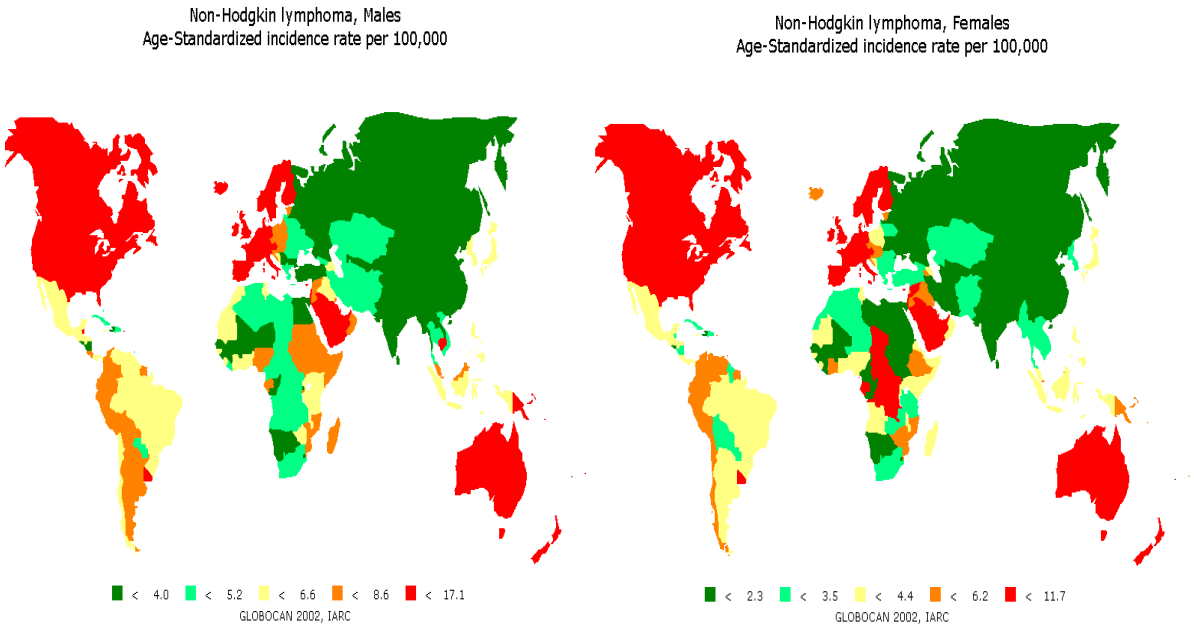
Who gets lymphoma?

- Increasing age
- Abnormalities of the immune system
  - Inherited
  - Related to treatment of another condition
  - Acquired (HIV)
- Viruses
  - Hepatitis B and C
  - Human herpes virus 6
- Exposure to certain chemicals
- Bacteria
  - Helicobacter pylori

Genetics?
Environment?
Diet/lifestyle?

Non-Hodgkin Lymphoma occurs worldwide but is more common in developed countries





Trends in Incidence, USA

International Variation

- 83% increase in age-adjusted incidence between 1975-2008

Slide courtesy of Dr. Brian Chiu

General approach to patient with lymphoma

What does the patient have?

DIAGNOSIS

How much disease does the patient have?

STAGING

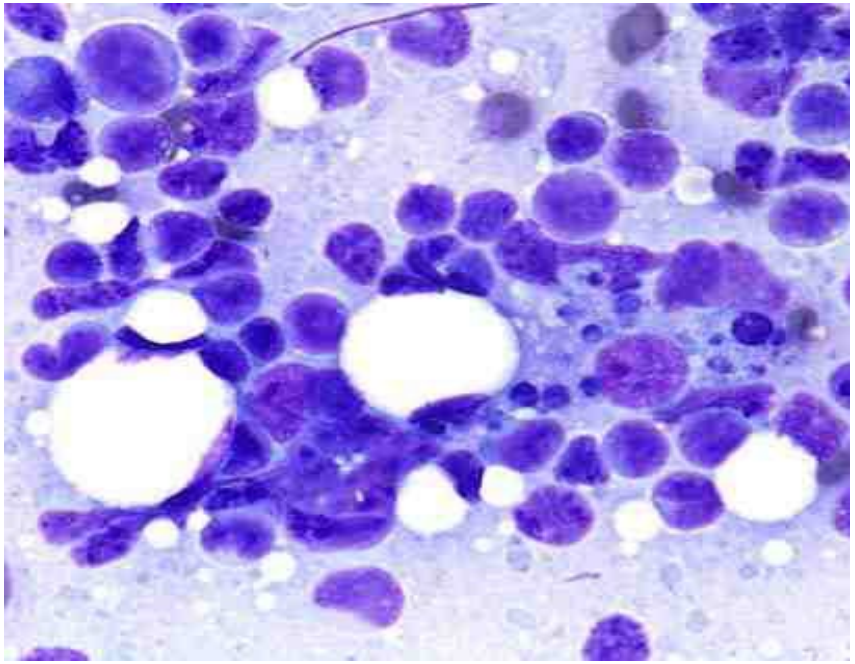
How will the patient

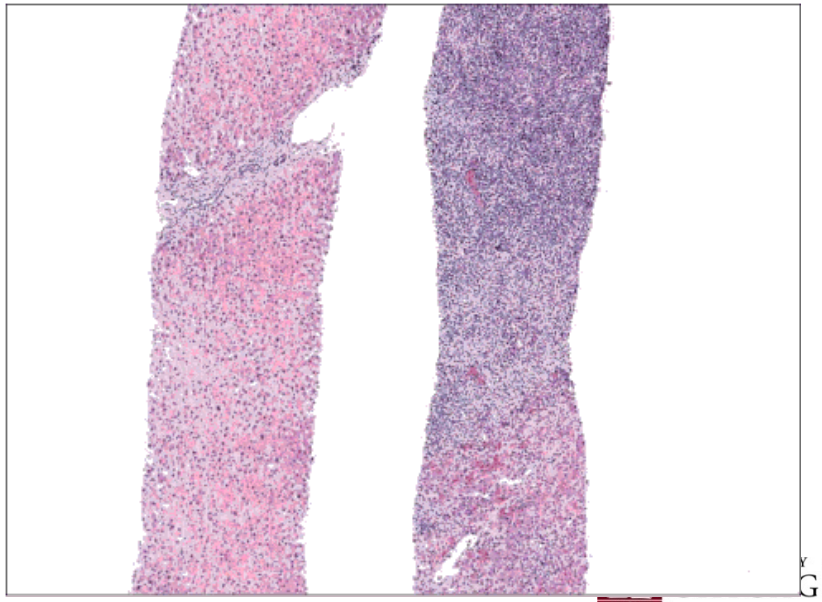
PROGNOSIS

How is lymphoma diagnosed?
TISSUE IS THE ISSUE

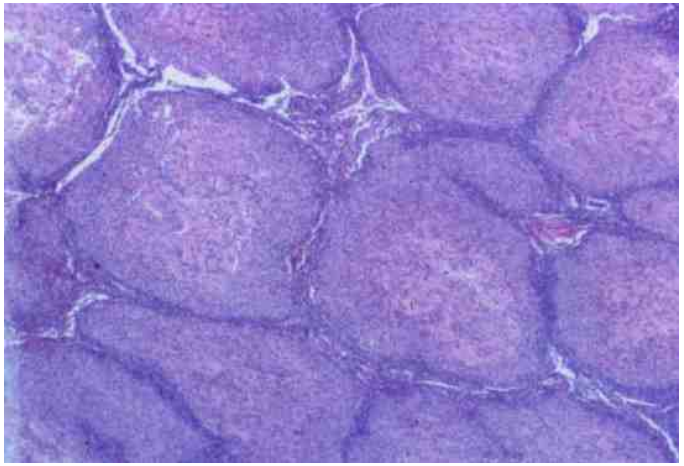
	PRO	CON
Fine needle aspirate	•can distinguish lymphoma from other cancers •Quick, easy, office-based	•Unable to give architectural detail •Insufficient for most prognostic tests
Core needle biopsy	•Can be done in hard to reach places (stomach, spinal cord)	•Unable to give architectural detail •Insufficient for most prognostic tests
Incisional or excisional biopsy	•Gold standard •Allows architectural evaluation •Allows tests for prognosis •Can be used for research	•May be more invasive •May require surgery and anesthesia

Relative sizes of biopsy material

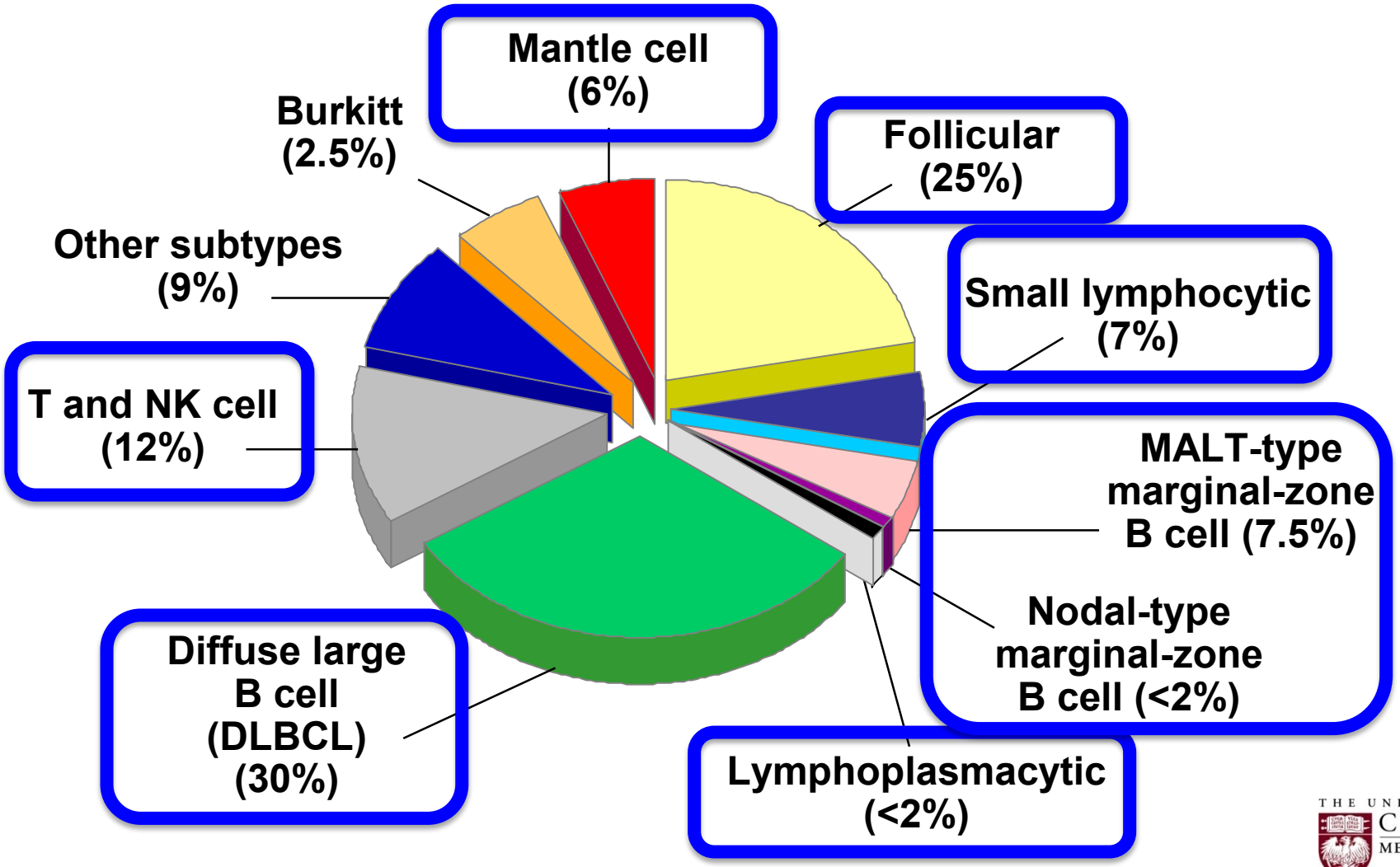




Excisional lymph node biopsy



There are more than 80 types of lymphoma



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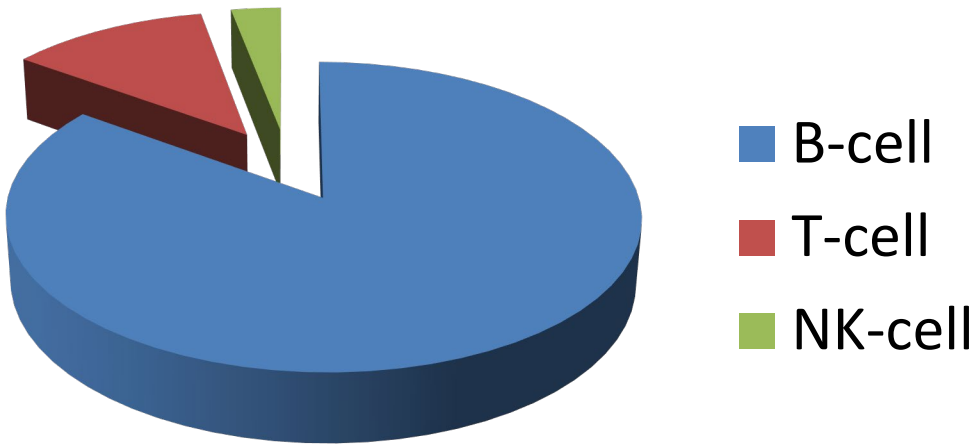
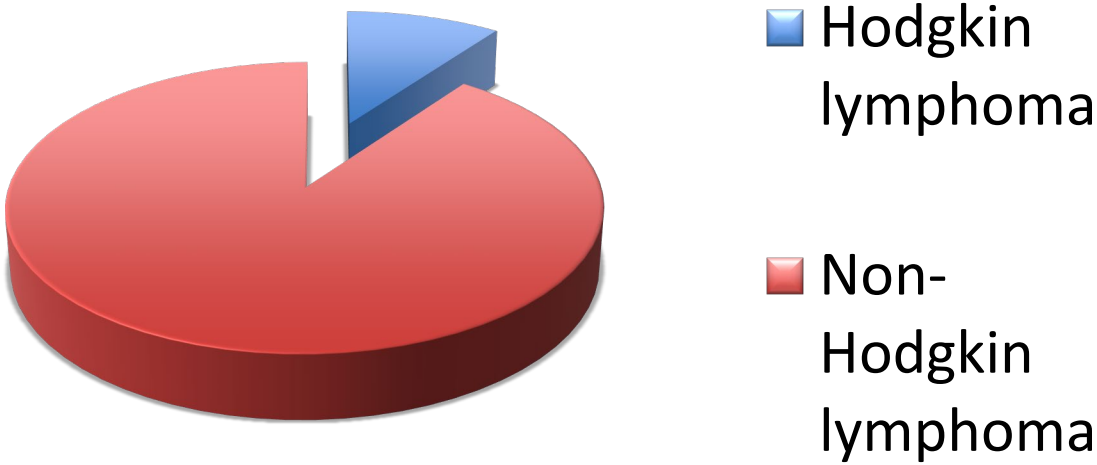
There are many ways to slice the “lymphoma pie”





How do we make sense of all these lymphoma types? Look at "expected clinical behavior"….

Low grade/indolent lymphoma

Mantle cell lymphoma?

Intermediate grade/aggressive lymphoma

T-cell lymphomas?

High grade/highly aggressive lymphoma

1. Slow growing
2. Incurable
3. More common in elderly

1. Fast growing
2. Potentially curable
3. Occurs in all age groups

1. Very fast growing
2. Some are highly curable

General approach to patient with lymphoma

What does the patient have?

DIAGNOSIS

How much disease does the patient have?

STAGING

How will the patient

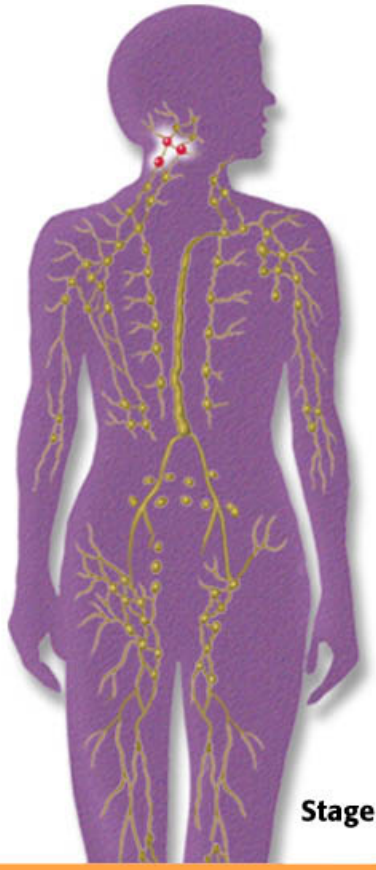
PROGNOSIS

Ann Arbor Staging: Stage I

Factors That Influence Treatment

Stage I

- Localized disease
- Single lymph node region
- Single organ outside of the lymph nodes



Courtesy of The Leukemia & Lymphoma Society.

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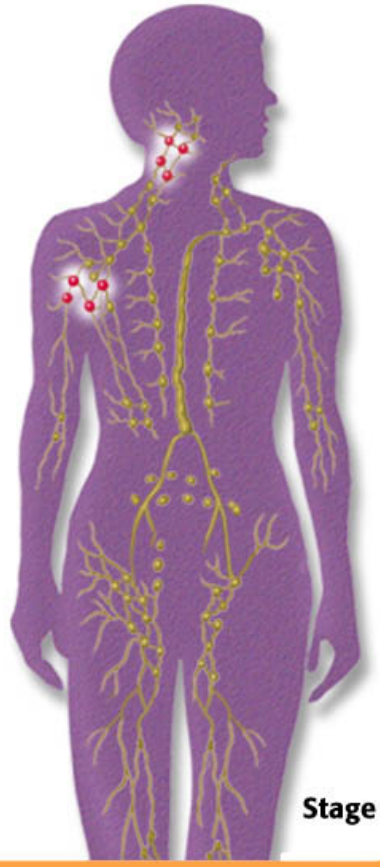
Ann Arbor Staging: Stage II

Factors That Influence Treatment

Stage II

- Two or more lymph node regions near to each other



Courtesy of The Leukemia & Lymphoma Society.

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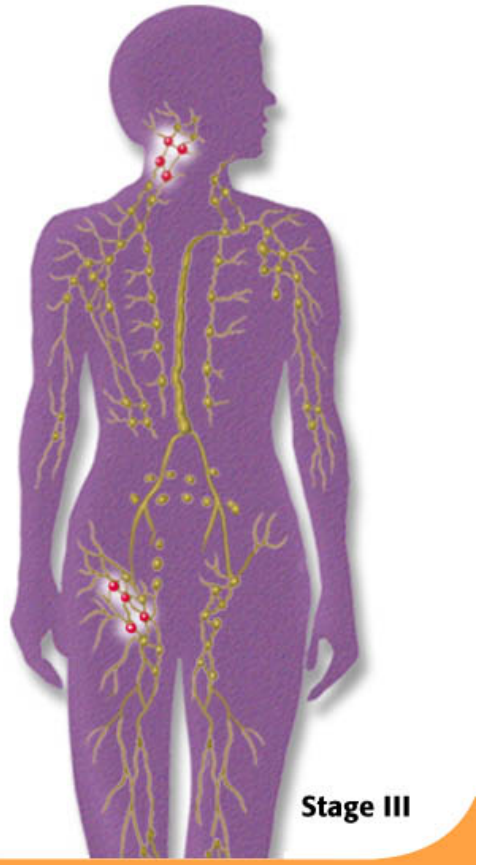
Ann Arbor Staging: Stage III

Factors That Influence Treatment

Stage III

- Two or more lymph node regions in different parts of the body



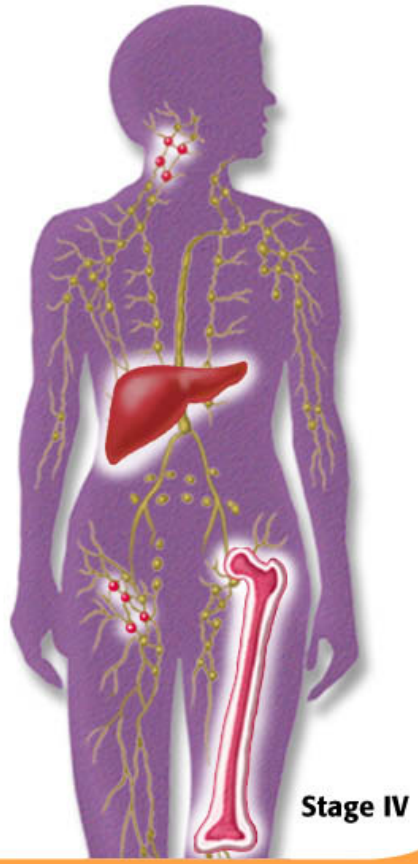
Courtesy of The Leukemia & Lymphoma Society.

Ann Arbor Staging: Stage IV

Factors That Influence Treatment

Stage IV

- Widespread disease
- Multiple organs
- With or without lymph node involvement



Courtesy of The Leukemia & Lymphoma Society.

What are “B symptoms”?

- Three classic B symptoms:
  - Fevers
  - Night sweats
  - Unintentional weight loss more than 10% of body weight
- Other parts of staging:
  - E: extranodal
  - X: bulky (> 10 cm in size)
  - S: spleen is involved
- Other symptoms that can happen with lymphomas:
  - Itching
  - Pain with alcohol intake
  - fatigue

Imaging: an important part of staging

CT Scans

(Computed tomography)

Gives STRUCTURAL information

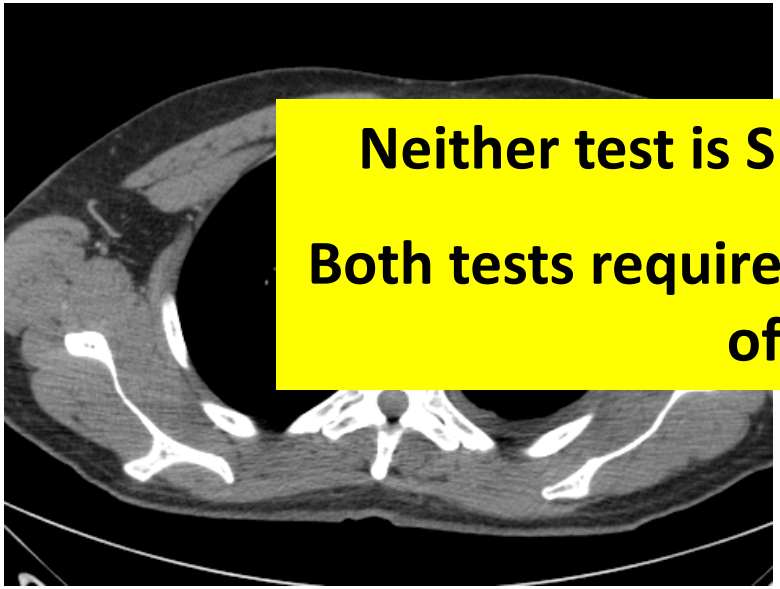
Allows measurements

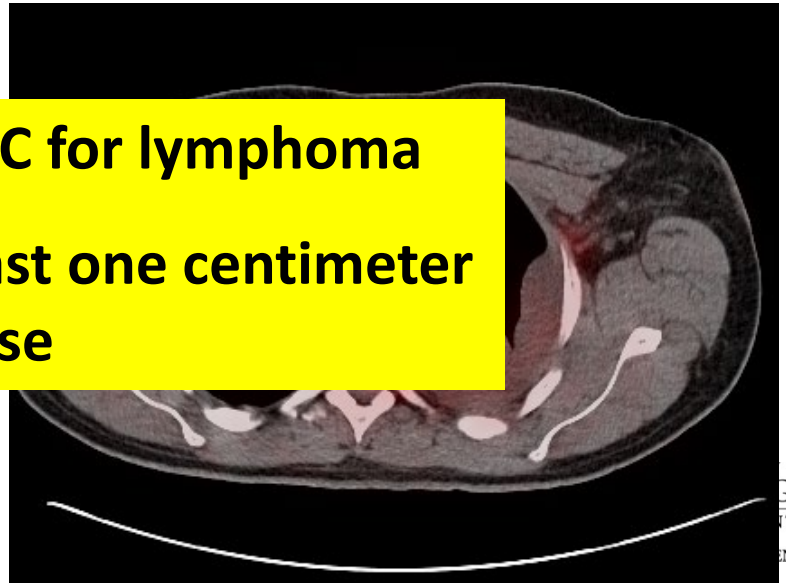
PET Scans

(positron emission tomography)

Gives METABOLIC information

Shows intensity of activity



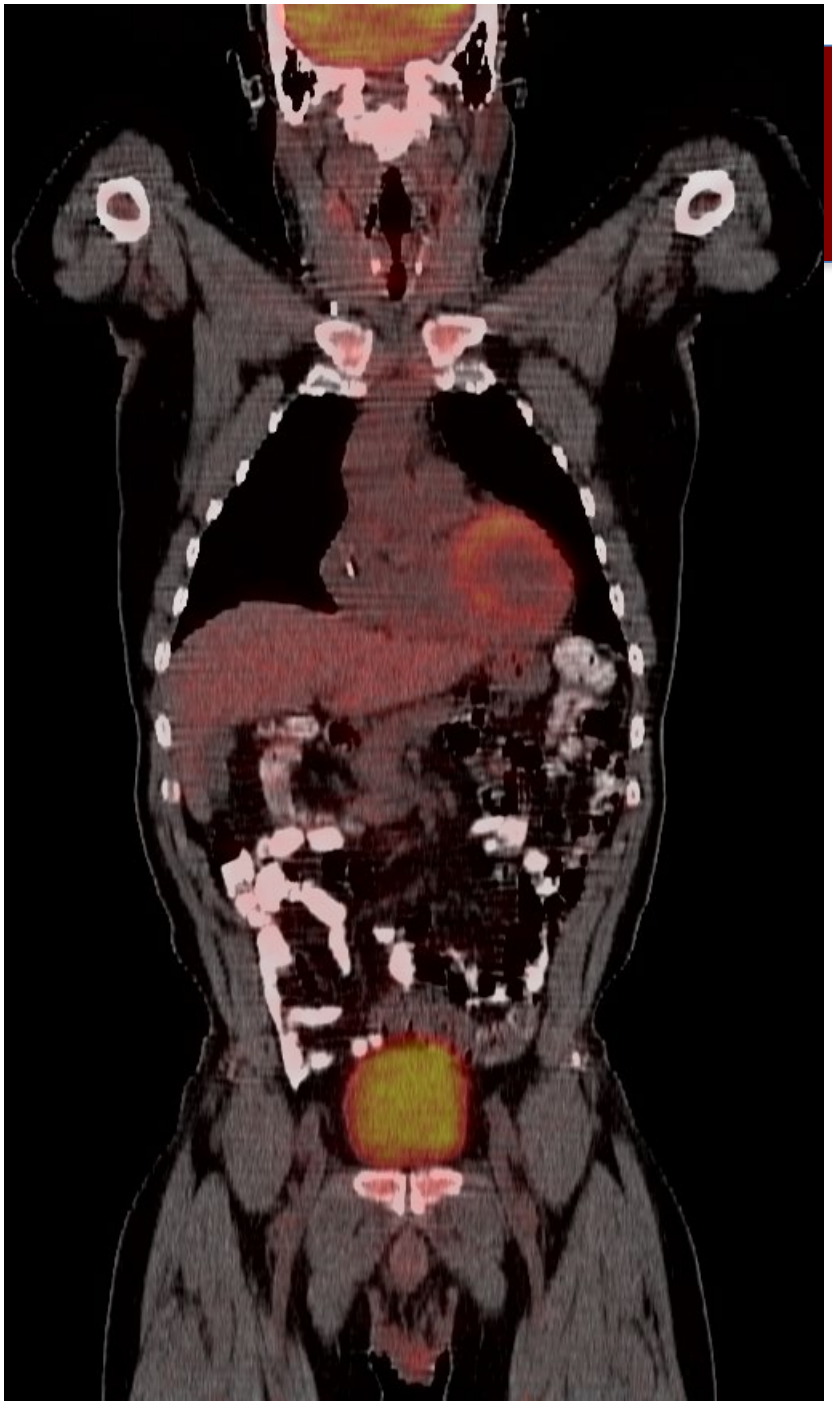


Neither test is SPECIFIC for lymphoma

Both tests require at least one centimeter of disease

PET/CT (4/07)

Post-treatment PET/CT (10/07)



Other types of initial tests that may be needed

- Bone marrow biopsy
  - Looks at the function of the bone marrow where all red cells, white cells and platelets are produced
  - Used less commonly than before
- Spinal tap (also called lumbar puncture)
  - Evaluates the fluid surrounding the brain and spinal cord
- Fertility preservation
  - Should be discussed with all patients of childbearing age
  - Consultation with specialists may be needed
- Echocardiogram or MUGA test
  - Performed to determine the heart's function before using certain chemotherapy treatments
- Pulmonary function tests
  - A test to evaluate the lung's capacity to extract oxygen from the air

General approach to patient with lymphoma

What does the patient have?

DIAGNOSIS

How much disease does the patient have?

STAGING

How will the patient

PROGNOSIS

Types of prognostic assessments

- Laboratory
  - LDH (lactate dehydrogenase)
  - B2M (beta-2 microglobulin)
- Clinical
  - IPI (International Prognostic Index)
  - FLIPI (Follicular Lymphoma International Prognostic Index)
  - MIPI (Mantle cell International Prognostic Index)
- Biological
  - Immunohistochemistry (protein analysis)
  - Cytogenetics, FISH (chromosome analysis)
  - Gene expression profiling

IPI (International Prognostic Index): diffuse large B-cell lymphoma

Age $\geq$ 60 years

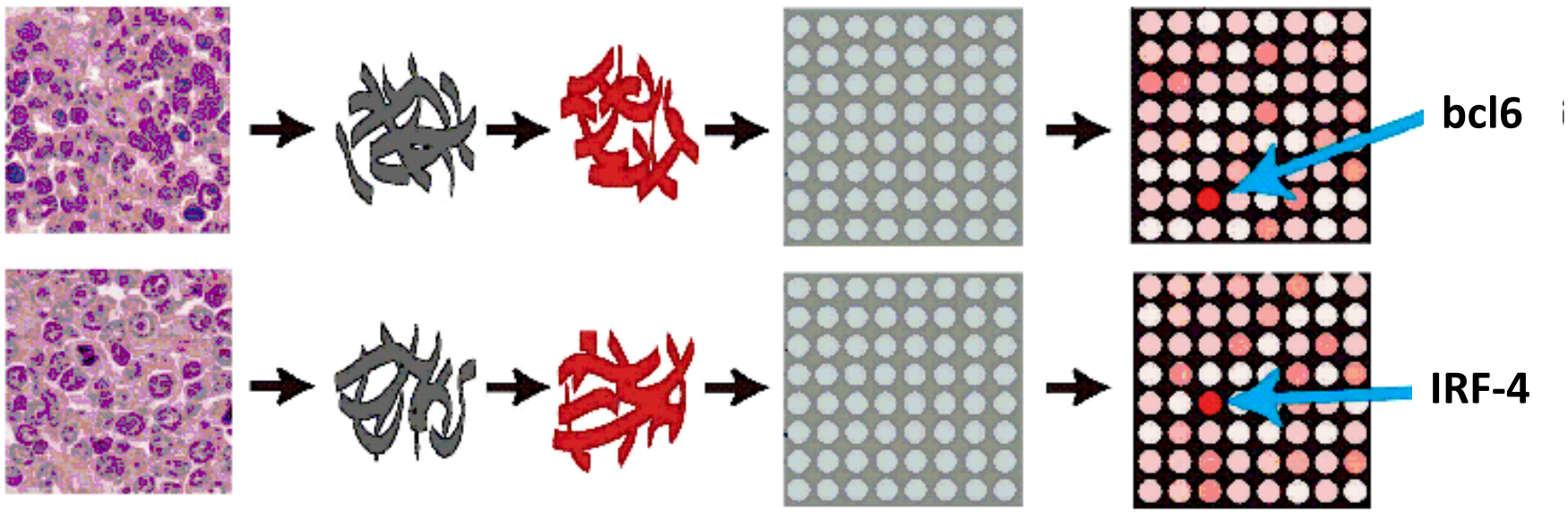
Performance status > 1

LDH abnormal

Stage 3 or 4 disease

More than one “extranodal” site

Why do patients have different outcomes?



Staudt LM. *N Engl J Med*. 2003;348:1777-1785.

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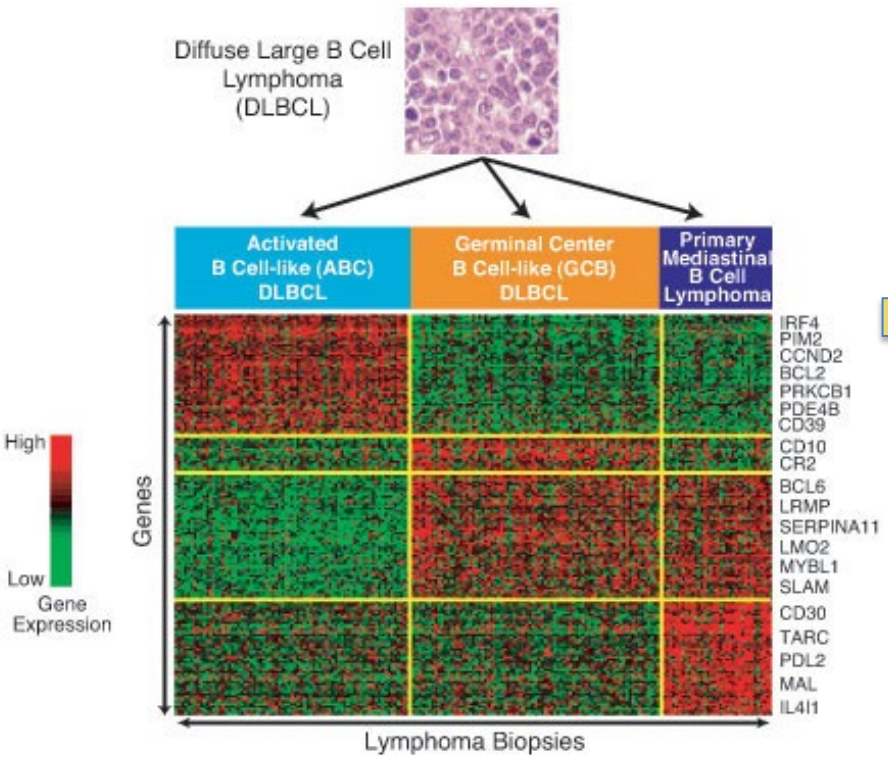
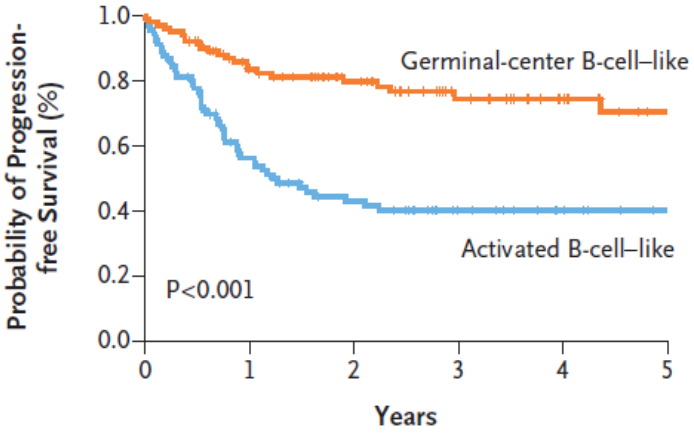
Why do patients have different outcomes?
GENE SIGNATURES





Two molecular subtypes with disparate outcomes

Lenz et al. *N Engl J Med.* 2008;359:2313-2323.

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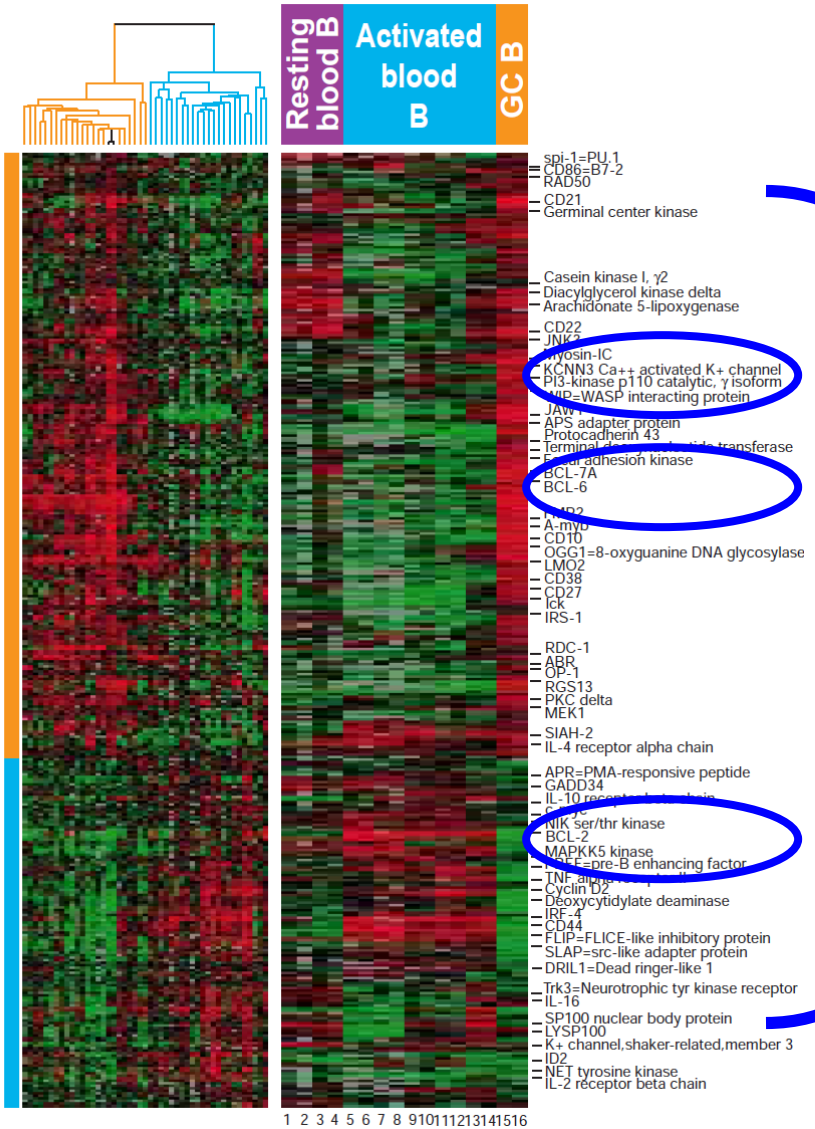
Understanding biology identifies targets



PI3K

BCL6

BCR signaling

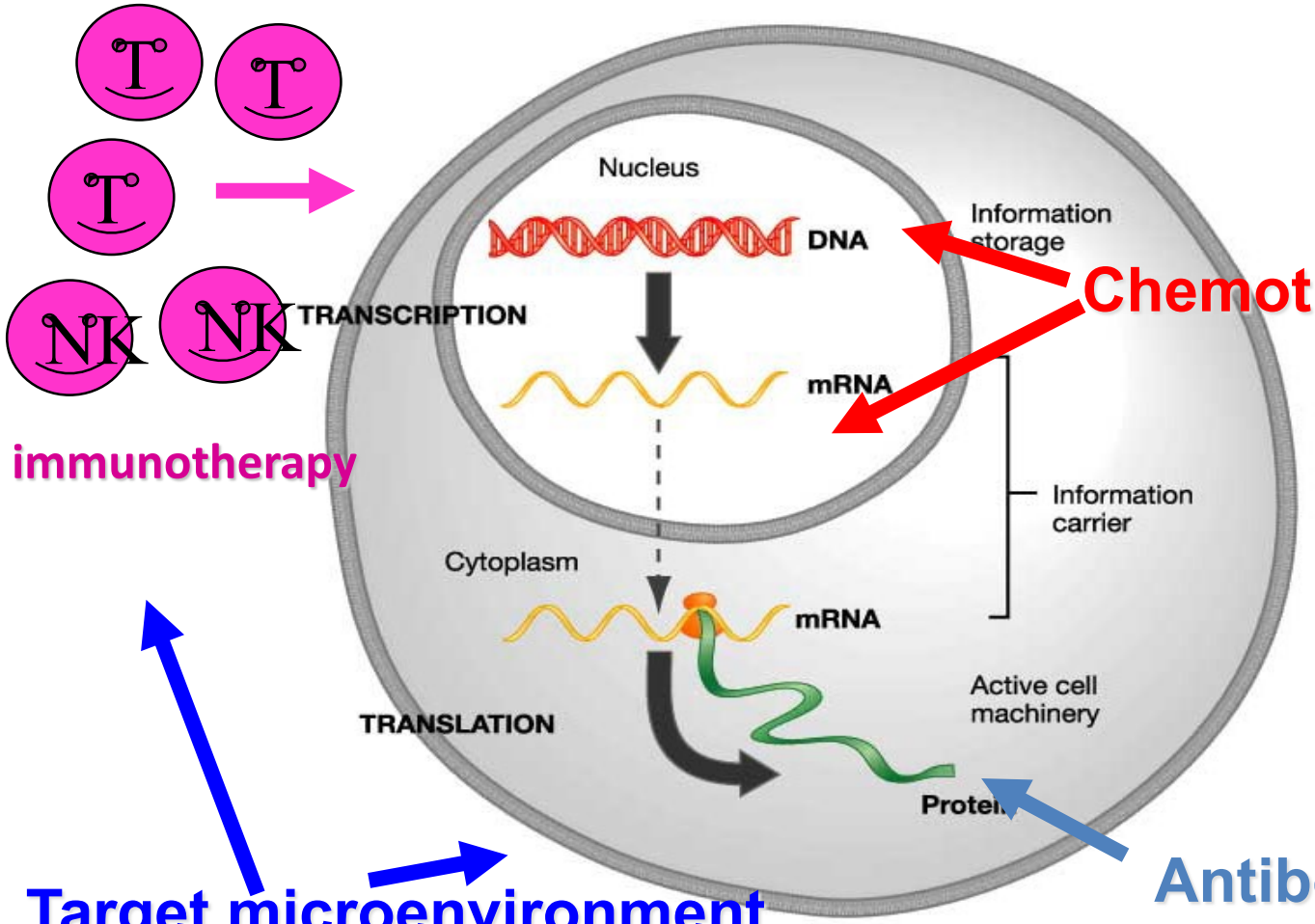
SYK

…and MANY more

Monti Blood. 2005 Mar 1;105(5):1851-61; Alizadeh Nature. 2000 Feb 3;403(6769):503-11

TYPES OF TREATMENT

Therapy and lymphoma cells



Chemotherapy drugs

immunotherapy

Target microenvironment

Antibodies,
Kinase inhibitors

Slide courtesy of Arnold Freedman

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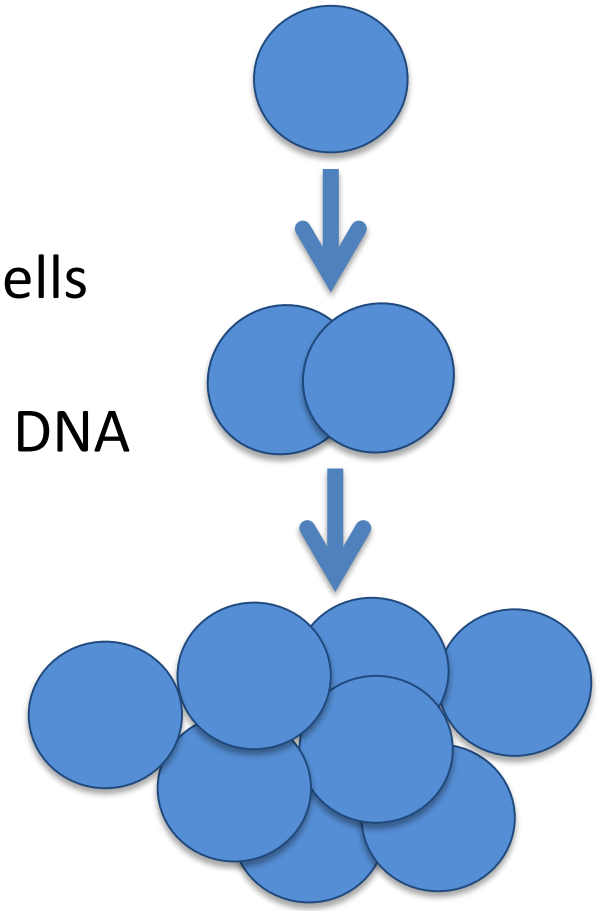
How do chemotherapy drugs work?

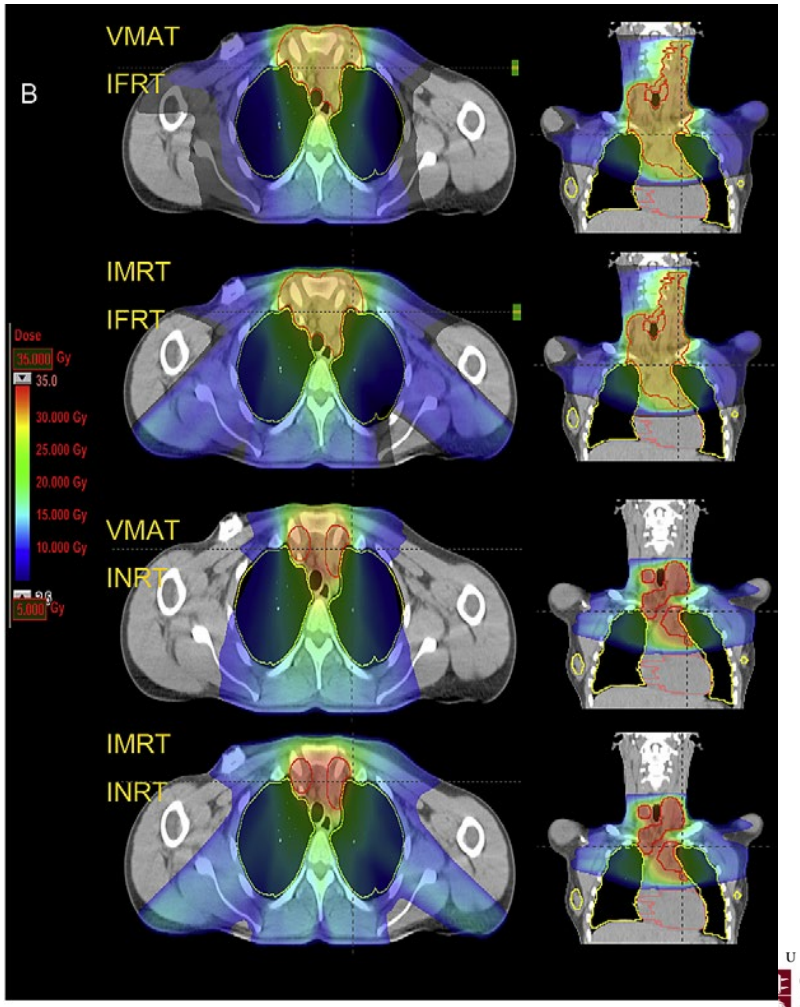
- Attack dividing cells
- Damage DNA
- Incorporate into DNA



- Collateral effects:
  - Hair loss
  - Bone marrow
  - Nails
  - Nerves

How does radiation work?

- Radiation attacks DNA in both normal and malignant cells
- ***SIZE*** and ***dose*** of radiation field affect side effects
- Role of radiation in lymphoma is shifting



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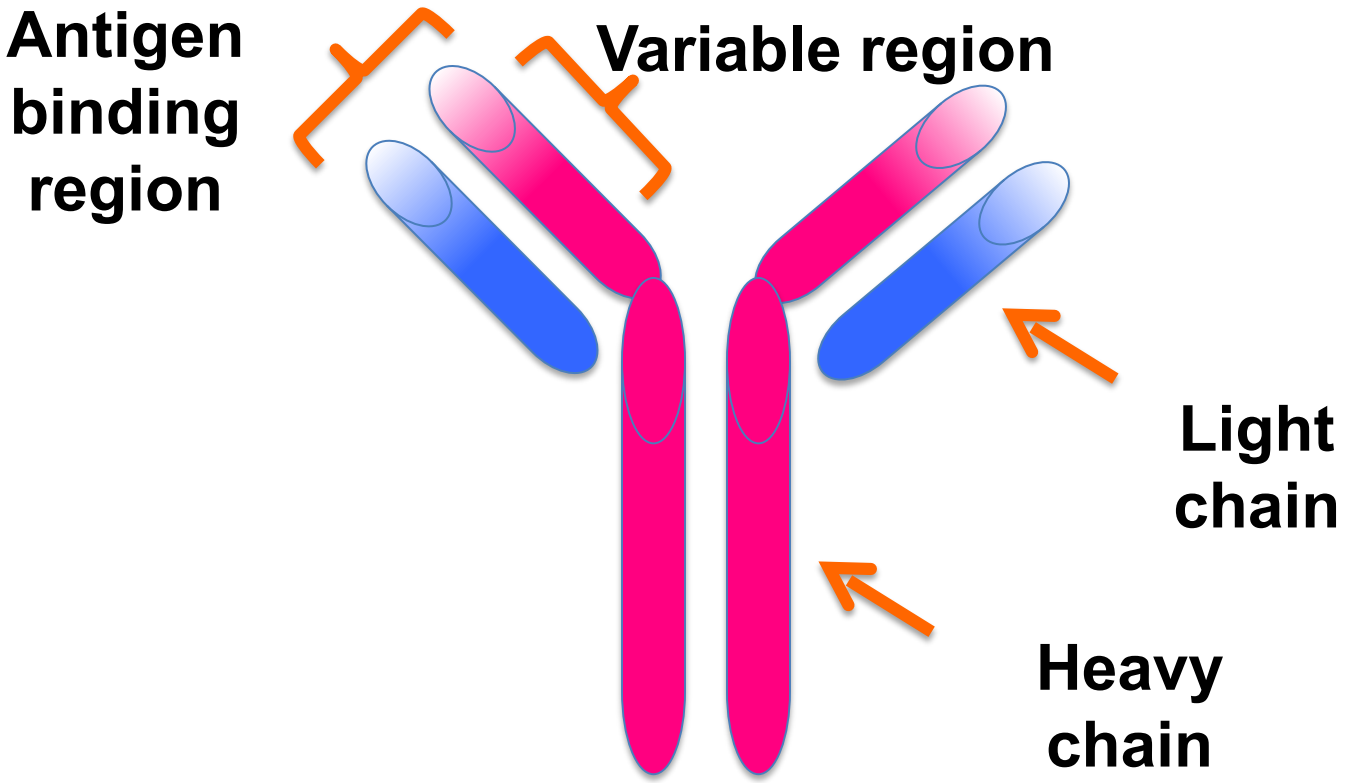
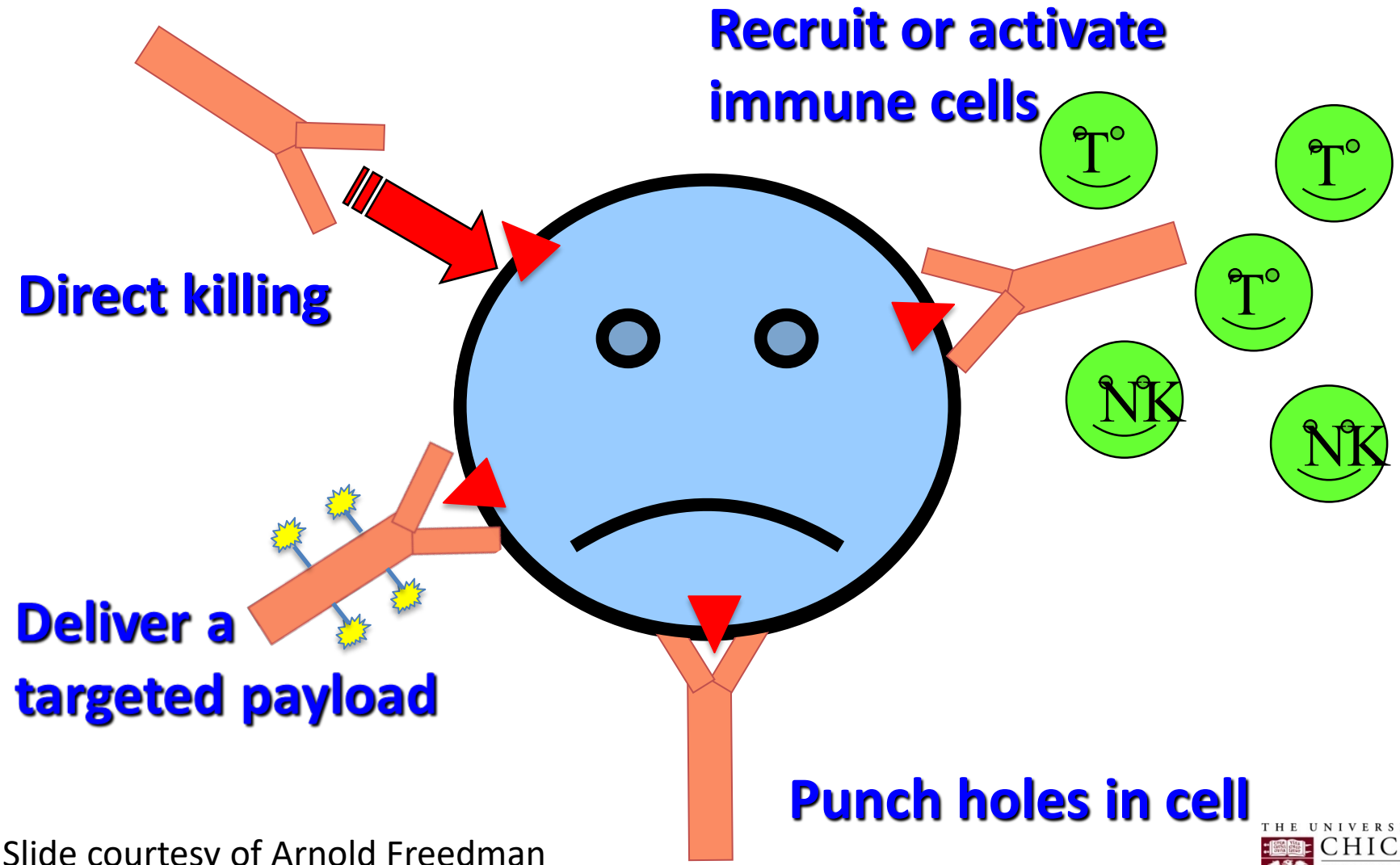
Monoclonal antibodies: a special type of protein made by B cells and plasma cells



How do antibodies kill lymphoma cells?



Slide courtesy of Arnold Freedman

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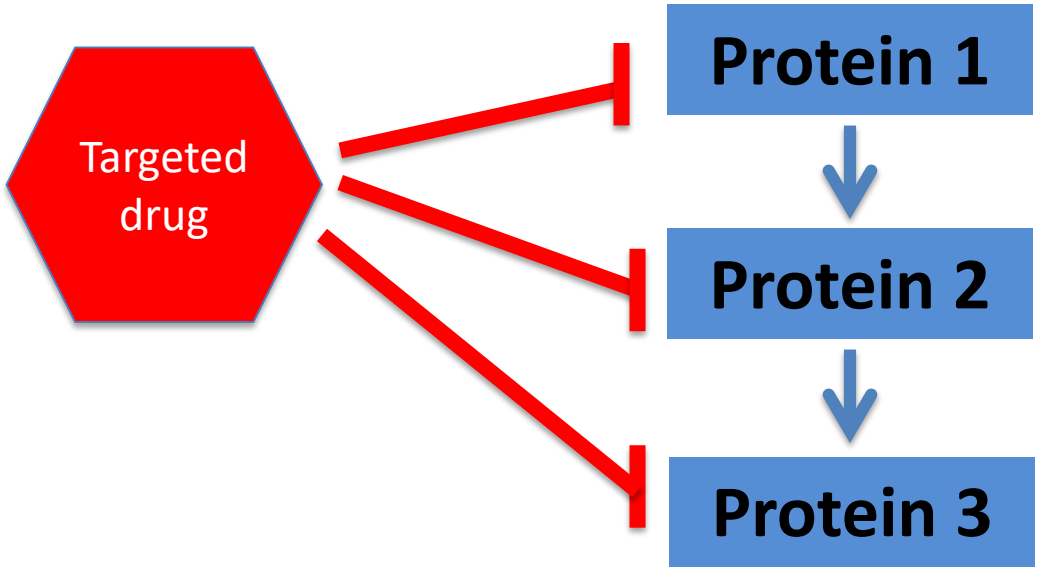
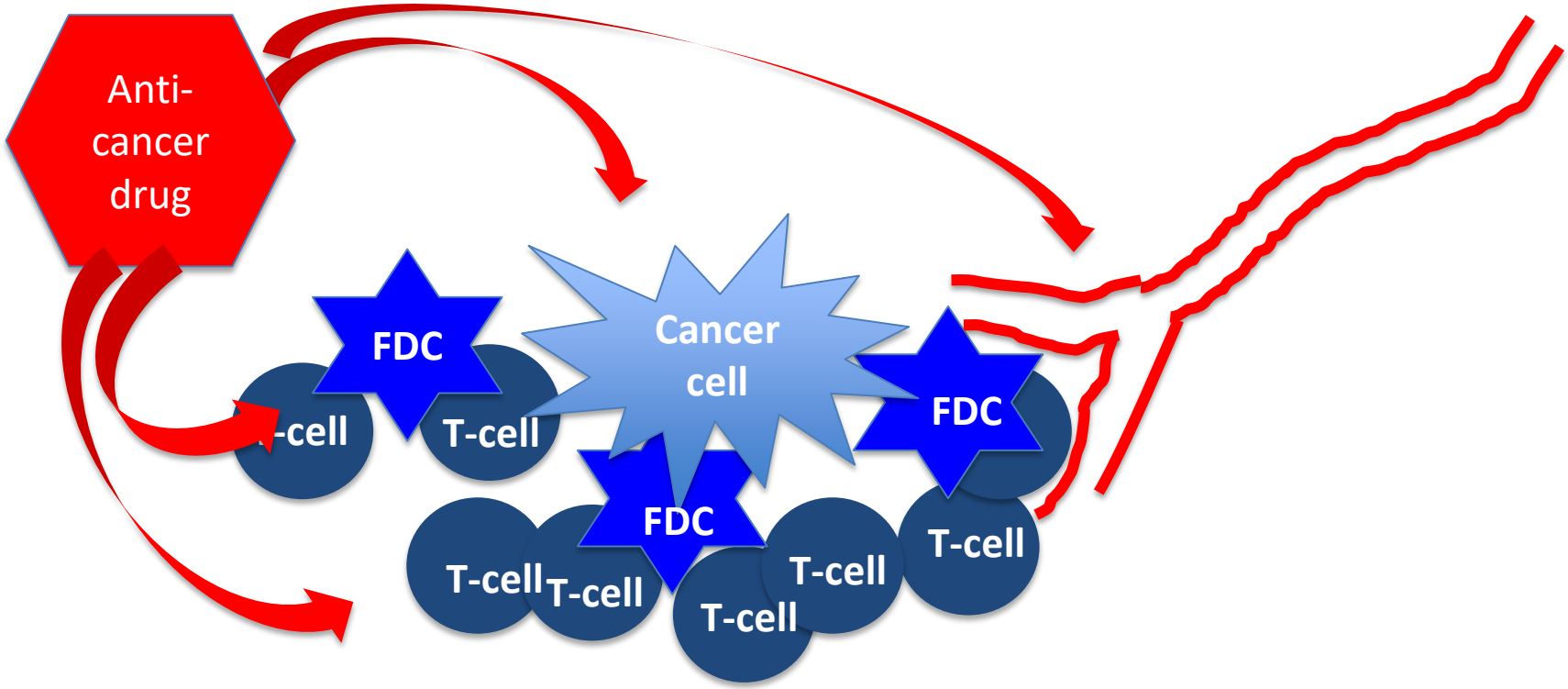
What are signaling pathways?

- Cascade of events inside a cell
- Usually cause cancer cells to grow and stay alive
- Can be targeted
- Some cancer cells are “addicted” to certain pathways

Signaling pathways: tell cancer cells what to do



Immunomodulatory agents: seed vs. soil



Immunotherapy, Stem cell transplant, CAR-T

- Harness the immune system to kill lymphoma cells
- Can use drugs (immunotherapy)
- Can use stem cells (stem cell transplant)
- Can use manipulated T-cells (CAR-T therapy)

Come to Immunotherapy Plenary Session on Sunday!!

Summary: Lymphoma Overview

- A complex family of blood cancers
- A good biopsy is CRITICAL for management
- We are just beginning to understand why lymphomas develop
- Staging and prognosis are important parts of the overall management
- There are MANY new treatments that are based on better science

Listen, learn, absorb and ask questions

Thank you!

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