

# **Immunohistochemistry in Lymphoid Neoplasms**

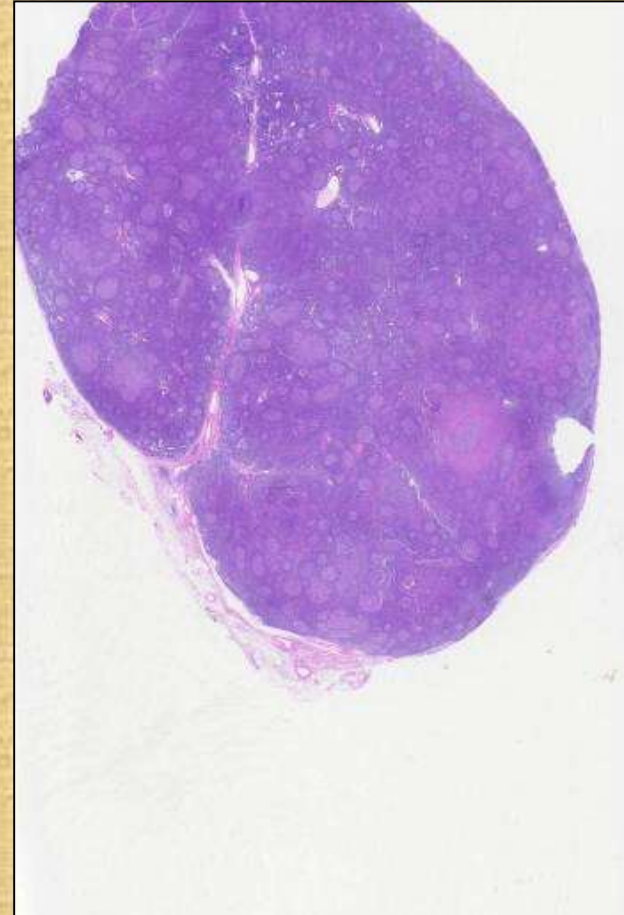
PRESENTED BY

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**Dennis P. O'Malley, MD**

# Larger Biopsies

Which would you rather diagnose?



# Little biopsy, little diagnosis?

- In some cases, a small sample can limit the quality or extent of examination
- We often use IHC stains to extend our interpretation in small samples
- Don't forget, you *can't diagnose what isn't there!*
- Do not be afraid to ask for more (or better) tissue!

# Patterns/Differential diagnosis

## Pattern

- Predominantly small lymphocytes
  - No discernable pattern
- Predominantly follicles
- Some follicles, some diffuse areas of small cells
- Mixed small and large cells; no pattern
- Mixed small and large; large cells localized
- Sinus pattern
- Increased stromal elements
  - Granulomas
  - Vascular elements
  - Fibrosis
- Polymorphous background/scattered very large cells
- Clusters/aggregates of large cells
- Sheets of large cells
- Interfollicular pale cells
  - Nodules
  - Diffuse

Small cell lymphoma

Hodgkin lymphoma

Large cell lymphoma

## Approach

T cell lymphoma

# My Basic Evaluation of Lymph Nodes by Immunohistochemistry...

## ...IS BASED ON FOUR APPROACHES

- Small B cell lymphoma
- Hodgkin lymphoma
- Large B cell lymphoma
- T cell lymphoma

NOTE: This is a “name” of an approach, and does not always indicate the exact diagnosis

# My Basic Evaluation of Lymph Nodes by Immunohistochemistry...

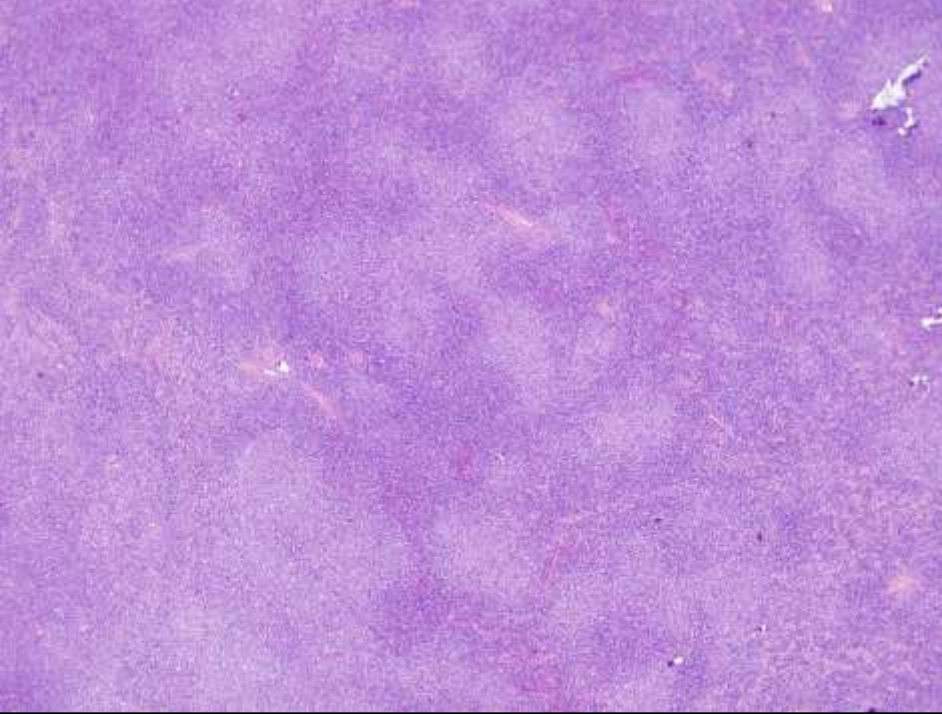
...IS BASED ON FOUR APPROACHES

- Small B cell lymphoma
  - Hodgkin lymphoma
  - Large B cell lymphoma
  - T cell lymphoma
- Individual variation or combination of evaluations
  - Distinctive evaluation for special circumstances

# Small B cell Lymphoma Approach

## When do I do it?

- Benign appearing nodes/normal architecture; e.g. **exclude lymphoma in benign appearing tissue**
- Follicles, normal or atypical
- Primary follicles/uniform small blue nodules
- Diffuse proliferations of predominantly small dark blue lymphocytes
- Features typical of small B cell lymphomas



Case 1:

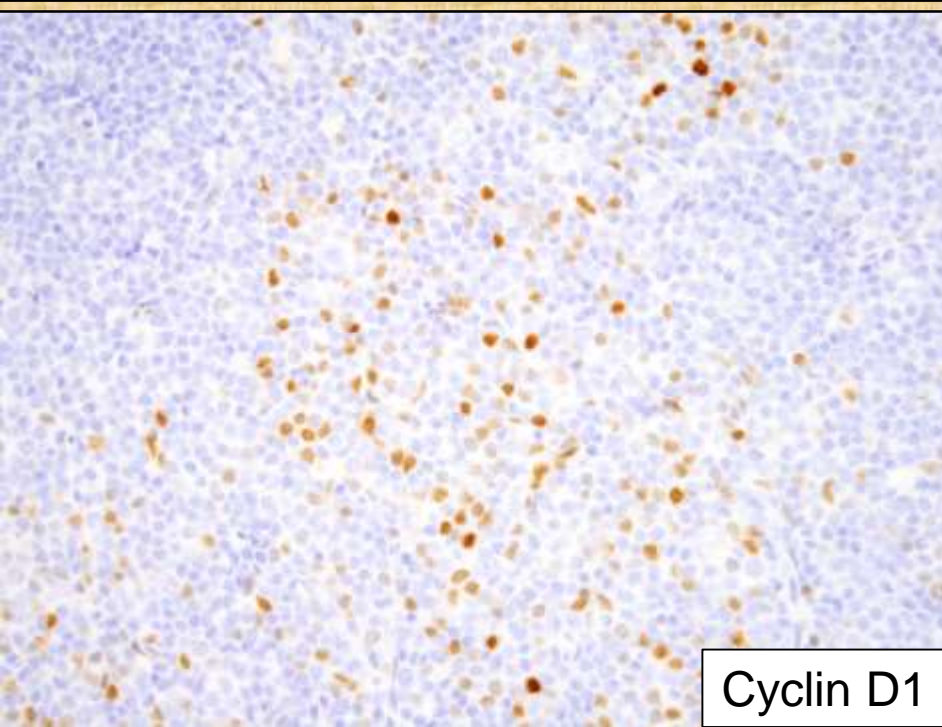
65 year old male presents with several month history of enlarged lymph node in neck. A biopsy was performed.

Q. The H&E and cyclin D1 immunohistochemical stain are presented. What additional studies should be performed?

A. FISH for IGH/CCND1

B. In situ staining for EBV

C. IHC for: CD5, CD20, CD3, BCL2, BCL6, LEF1, Ki67



Cyclin D1



# Small B cell Lymphoma Approach

## What do I do?

- CD3
- CD20
- CD5
- Cyclin D1
- BCL2
- BCL6
- Ki67
- LEF1

# Small B cell Lymphoma Approach

## What do I do?

- **CD3**
- **CD20**
- CD5
- Cyclin D1
- BCL2
- BCL6
- Ki67
- LEF1

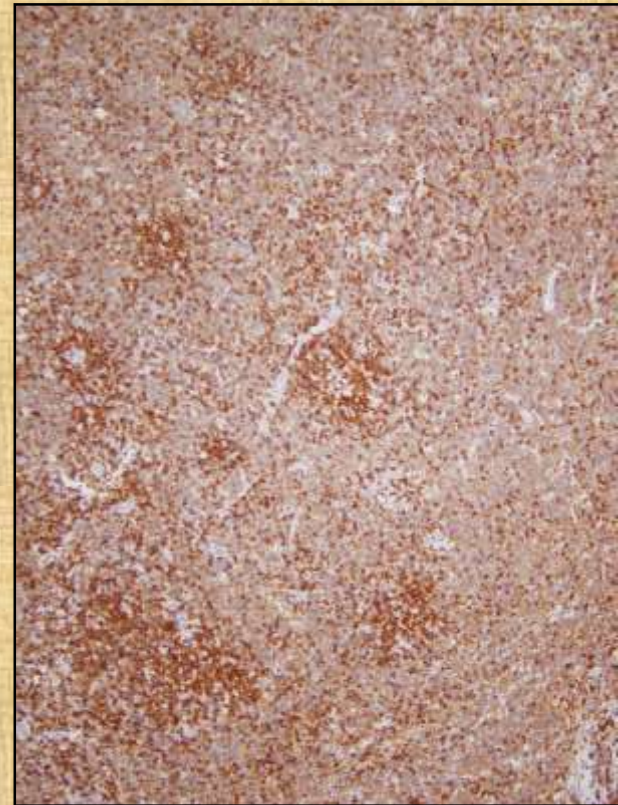
This combination is optimal in evaluating distribution of both normal and non-neoplastic T and B cells

# Small B cell Lymphoma Approach

## What do I do?

- CD3
- CD20
- **CD5**
- Cyclin D
- BCL2
- BCL6
- Ki67
- LEF1

B cells: Co-expression in a B cell population (comparison to CD20), would support a CD5 positive B cell lymphoma  
T cells: Loss of CD5 in T cells (comparison to CD3) would suggest or support a diagnosis of a T cell lymphoma



Variation in CD5 intensity in MCL versus normal T cells

CD3 = CD5. If not, then either abnormal T or abnormal B cells!

# Small B cell Lymphoma Approach

## What do I do?

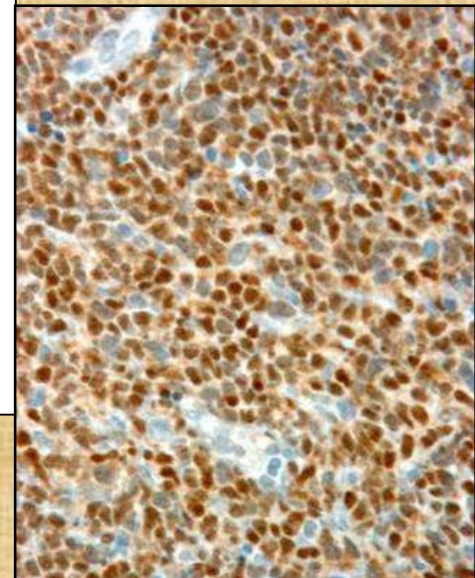
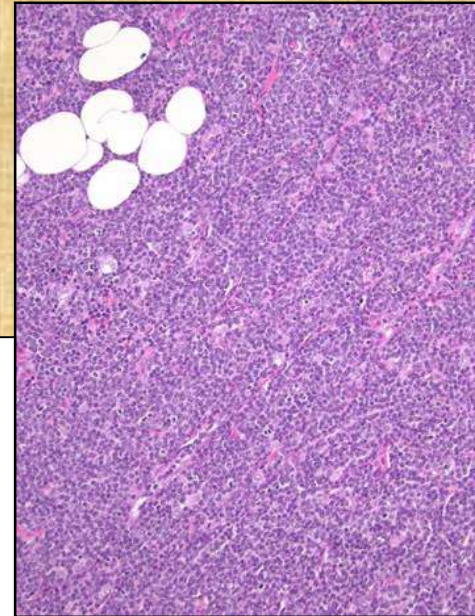
- CD3
- CD20
- CD5
- **Cyclin D1**
- BCL2
- BCL6
- Ki67
- LEF1

B cells: if positive, then diagnosis is most likely

**MANTLE CELL LYMPHOMA**

Other less likely possibilities include: hairy cell leukemia (weaker more variable staining), myeloma (plasma cell morphology)

Caveats: Endothelial cells will often express cyclin D1. Proliferating epithelial cells (all sites) will express nuclear cyclin D1



**Cyclin D1**

# Small B cell Lymphoma Approach

## What do I do?

- CD3
- CD20
- CD5
- Cyclin D
- **BCL2**
- BCL6
- Ki67
- LEF1

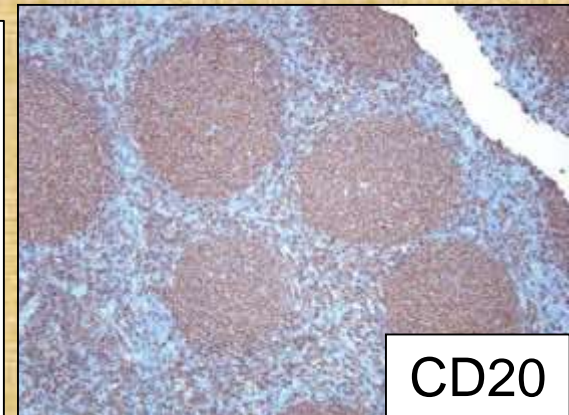
B cells: expressed in most normal B cells, except cells of reactive germinal center

Expressed in most small B cell lymphomas (>75%)

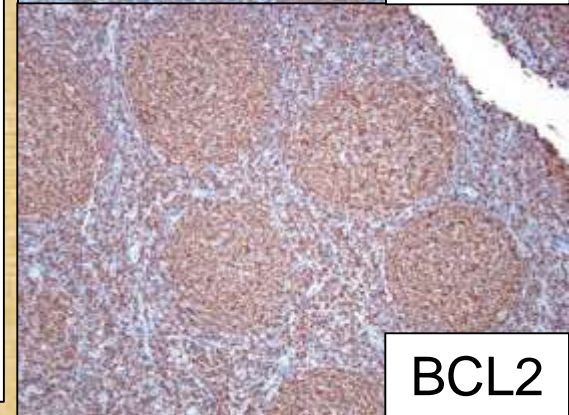
Expressed in most normal T cells. Loss of expression in T cells can suggest T cell lymphoma

Caveat: Expression in follicles should be compared to T cell markers. T cells will be positive and depending on number in follicle may lead to misinterpretation.

FOLLICULAR  
LYMPHOMA



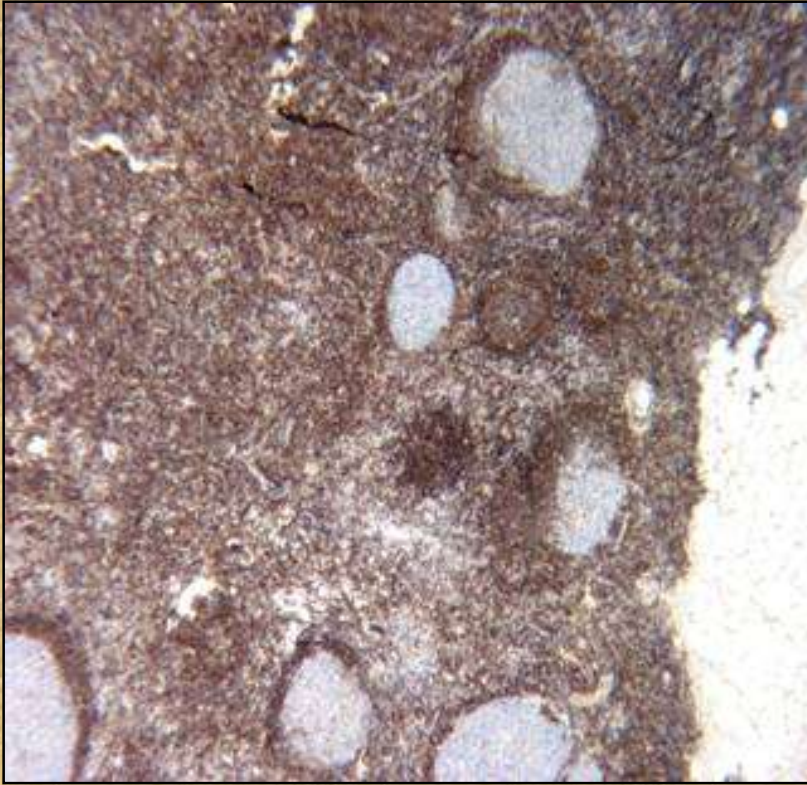
CD20



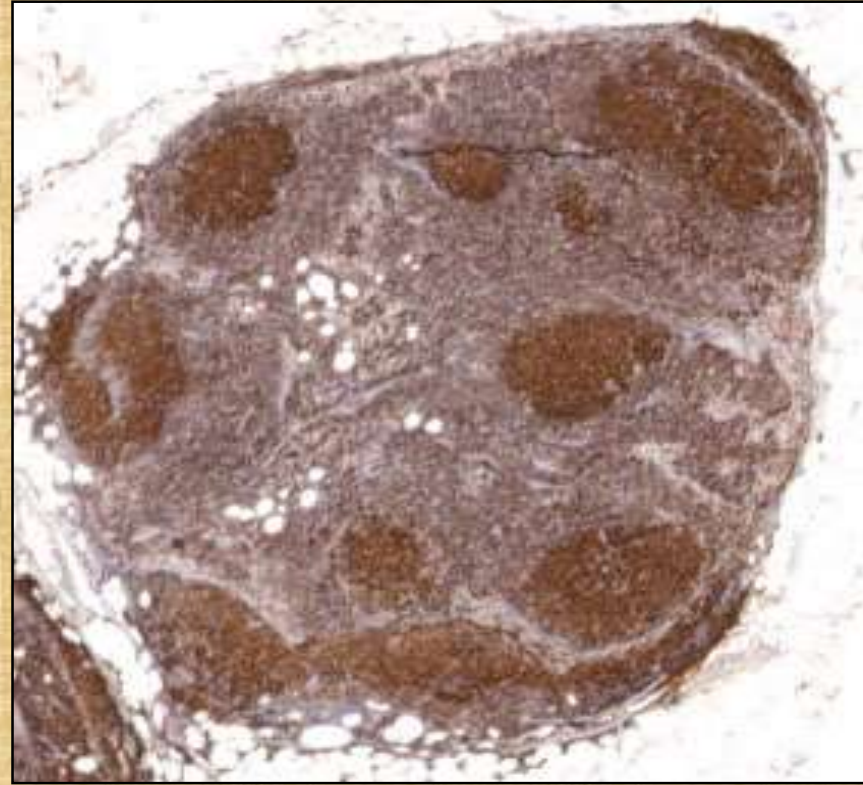
BCL2

# BCL-2

## Benign vs. Malignant Follicles

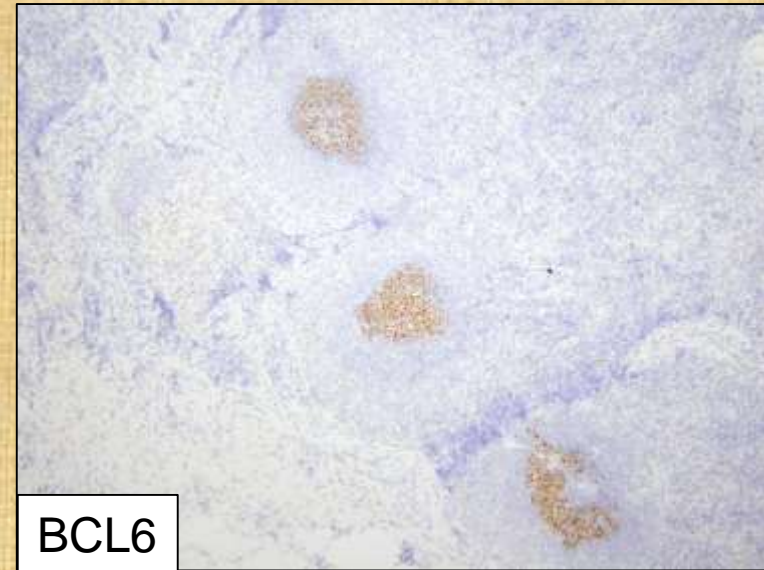
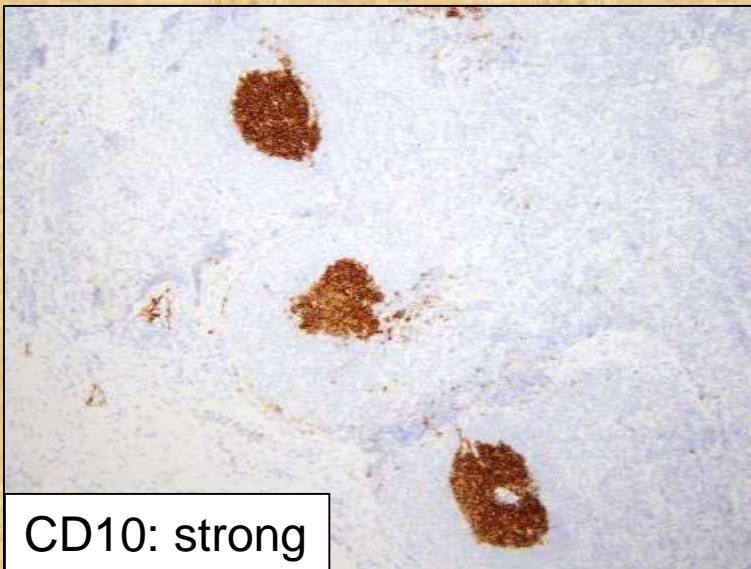
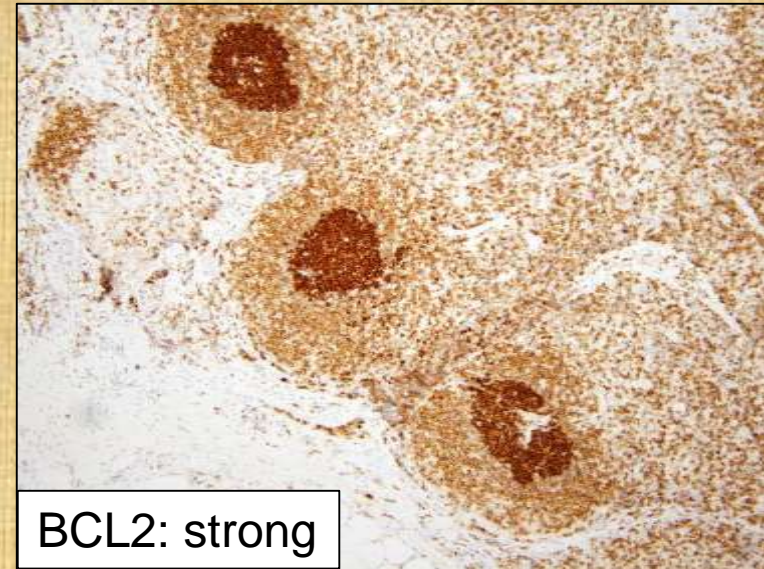
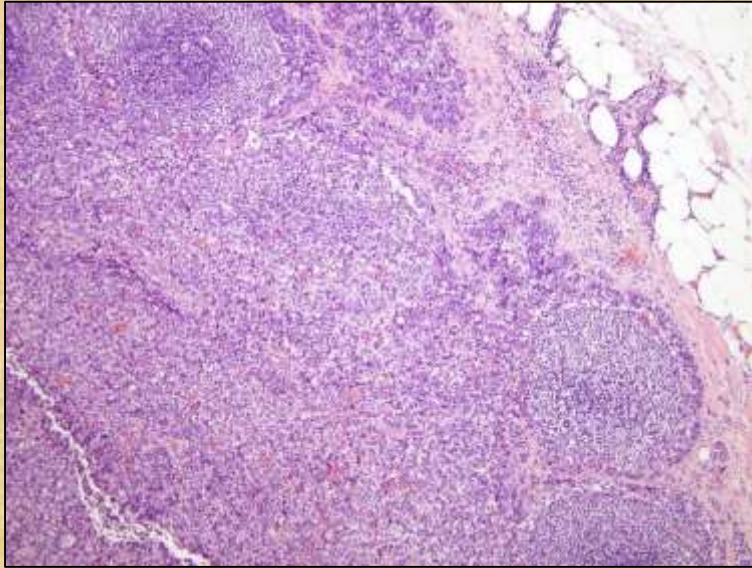


Follicular hyperplasia



Follicular lymphoma

# In situ follicular neoplasia



# Small B cell Lymphoma Approach

**BCL6**

## What do I do?

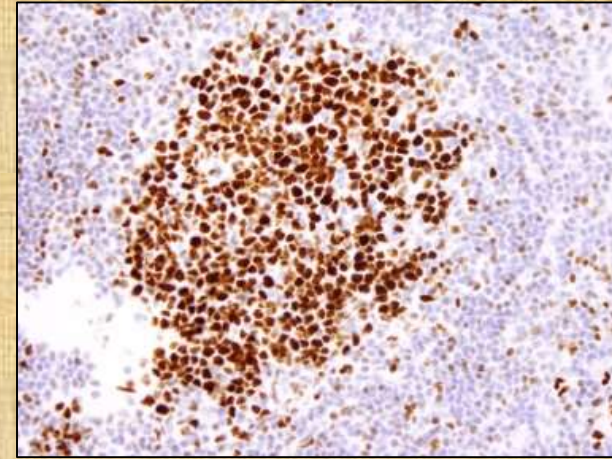
- CD3
- CD20
- CD5
- Cyclin D1
- BCL2
- **BCL6**
- Ki67
- LEF1

Highlights lymphocytes of follicle center origin

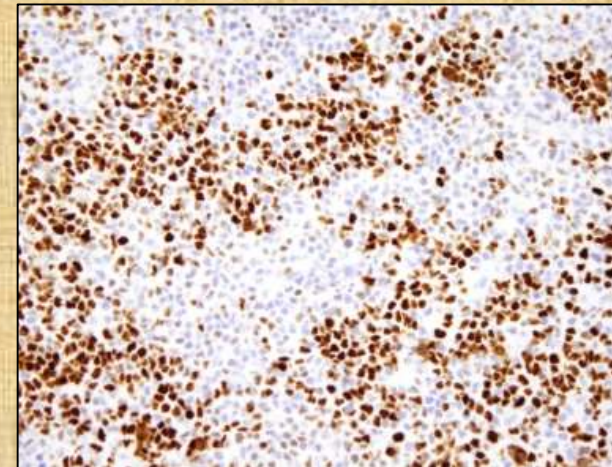
Nuclear staining

Does not stain stroma (in contrast to CD10)

Can highlight follicles, follicular colonization, abnormal distribution of follicle center cells



Follicle center



Follicular colonization



# Small B cell Lymphoma Approach

## What do I do?

- CD3
- CD20
- CD5
- Cyclin D1
- BCL2
- BCL6
- Ki67
- **LEF1**

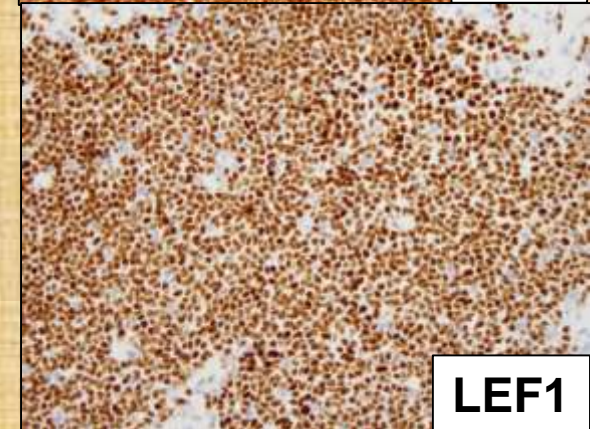
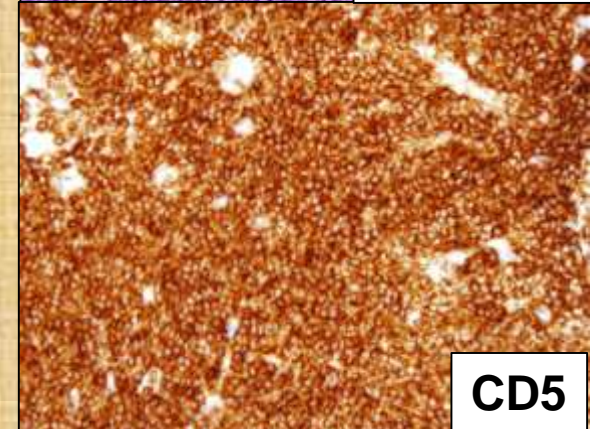
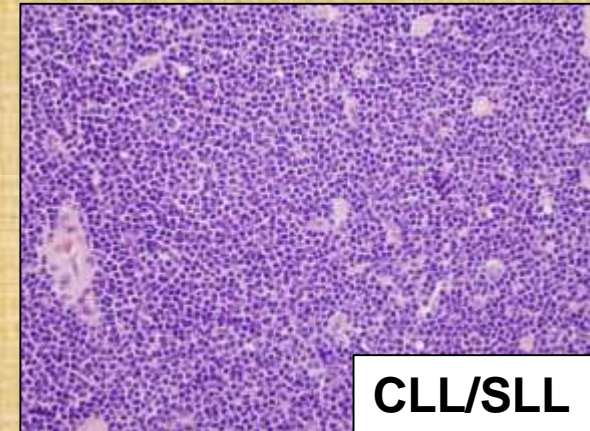
LEF1 is a pan T cell antigen stain

LEF1 absence in T cells may indicate abnormal, neoplastic T cells

LEF1 expression in B cells is NOT NORMAL

LEF1 expression in small B cells is **VERY LIKELY** to represent CLL, even in cases that are CD5 negative

LEF1 expression can be seen in DLBCL (3%); it can be seen in large cell transformation of CLL (Richter syndrome), but can also be seen in de novo DLBCL



# Small B cell Lymphoma Approach

## What do I do?

- CD3
- CD20
- CD5
- Cyclin D1
- BCL2
- BCL6
- **Ki67**
- LEF1

Pattern of proliferation can be used to determine normal or abnormal proliferation  
Can show distinctive findings in lymphomas

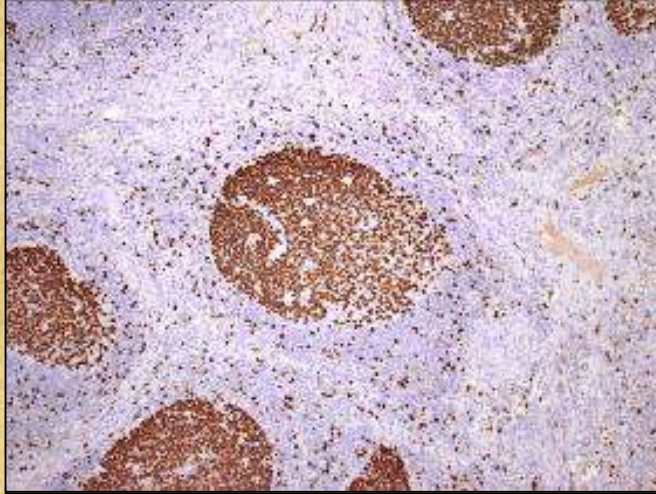
Evaluate normal vs. abnormal follicles

Evaluate for follicular colonization

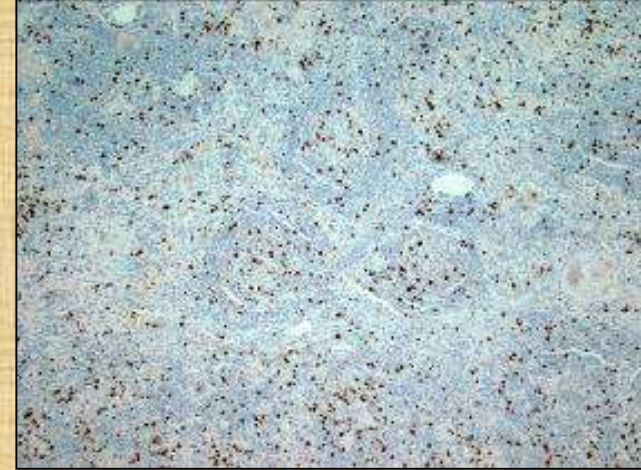
Pattern for CLL/SLL

Abnormal high proliferation (High grade or large cell?)

Normal



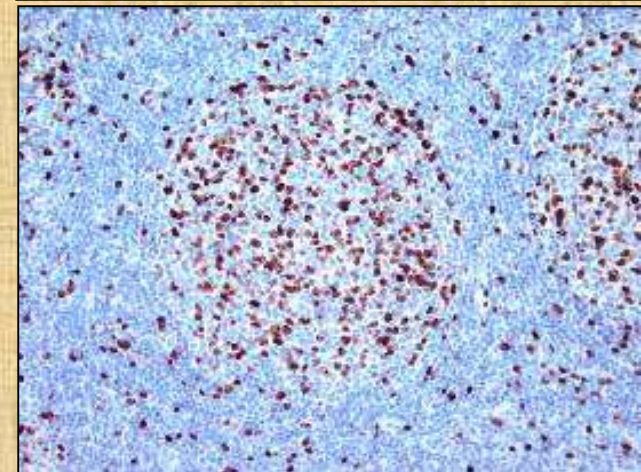
FL grade 1



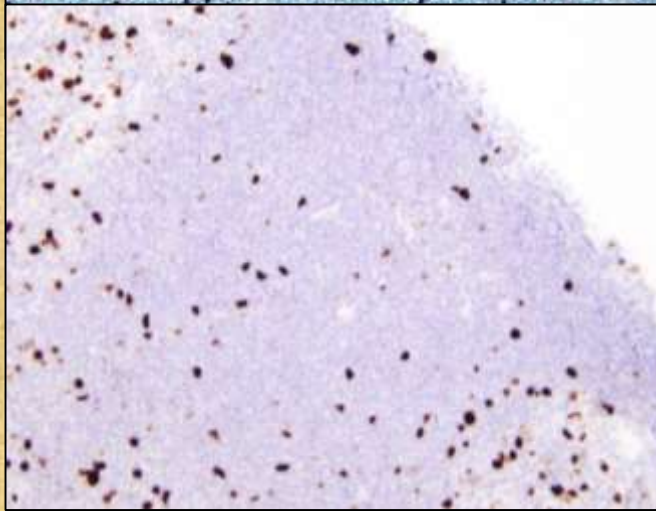
SLL –  
pseudofollicle



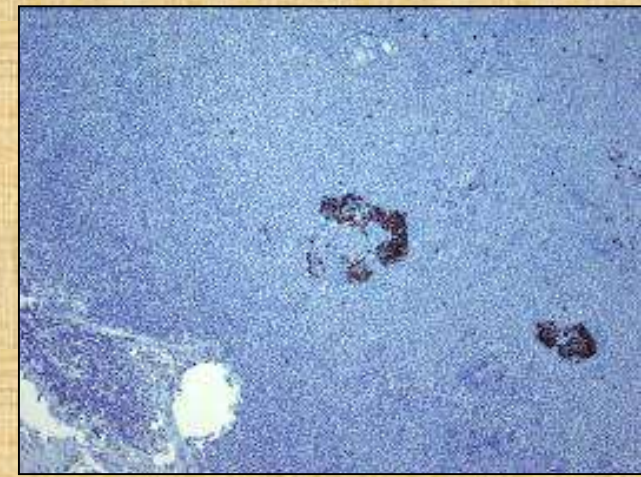
FL grade 2

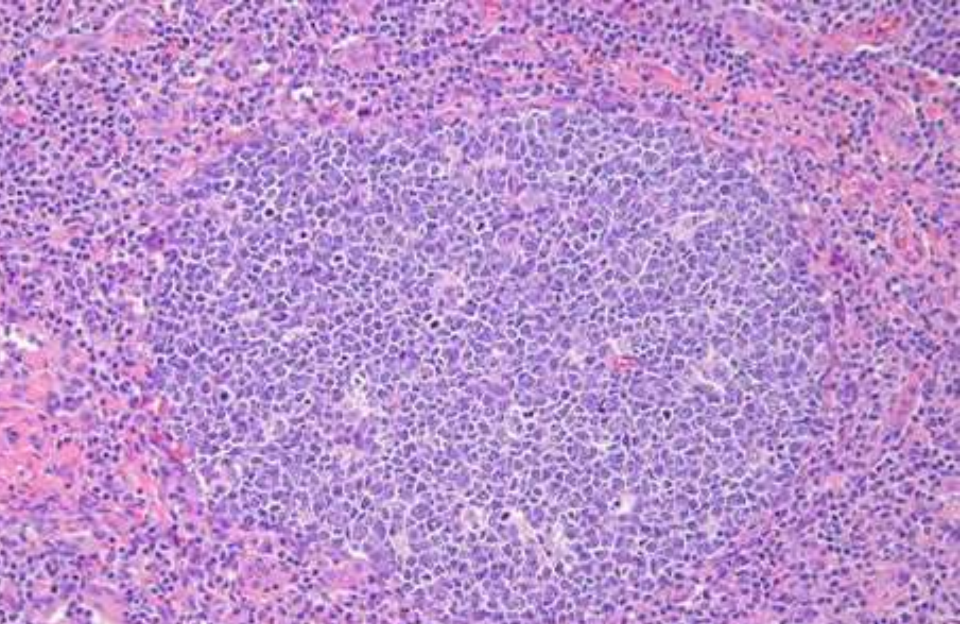


HV Castleman

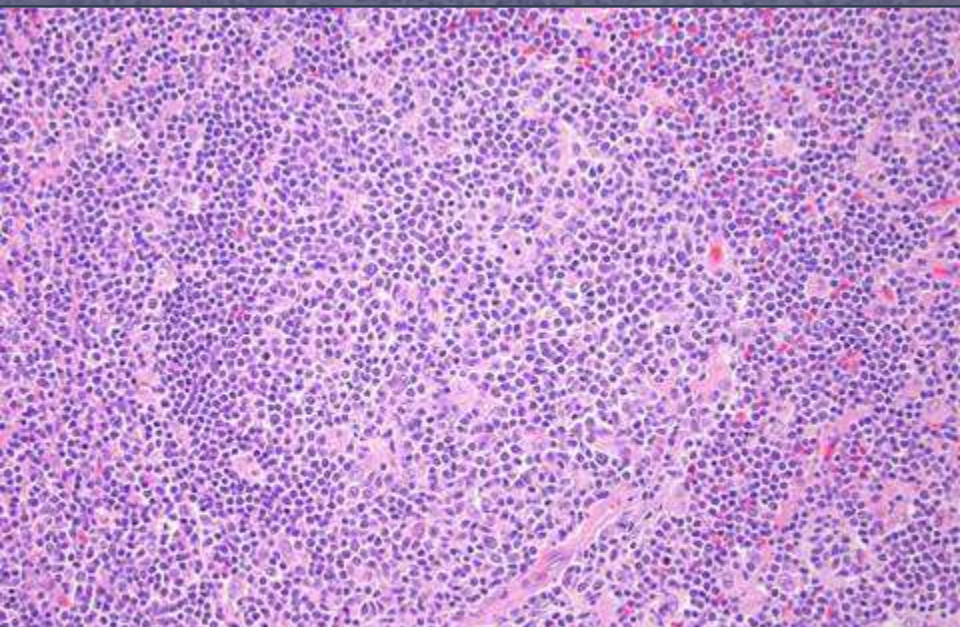


MZL with  
follicular  
colonization

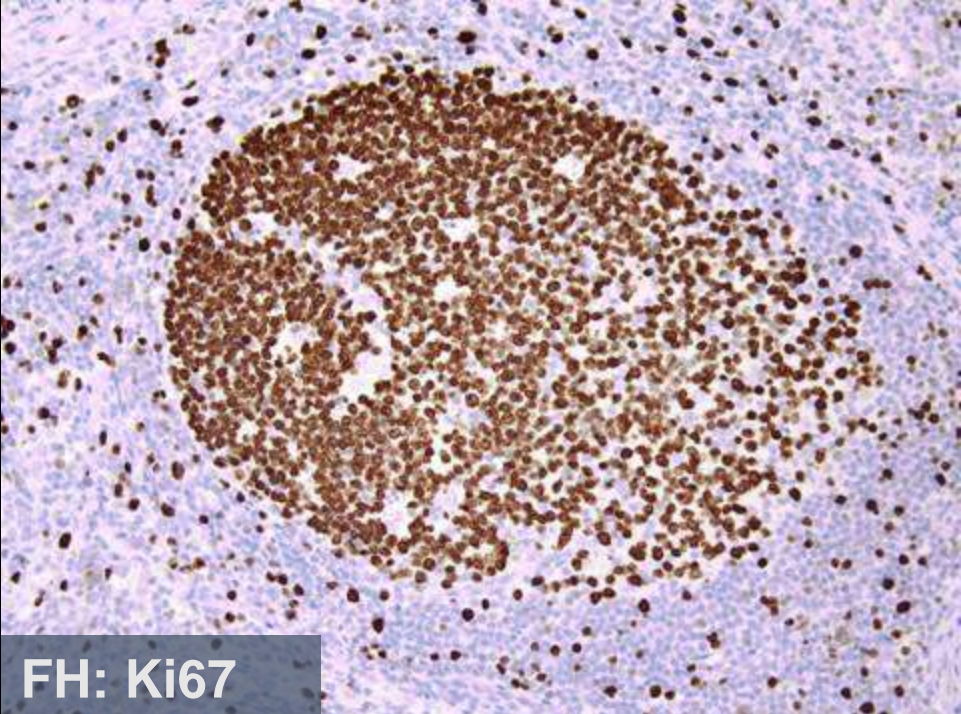




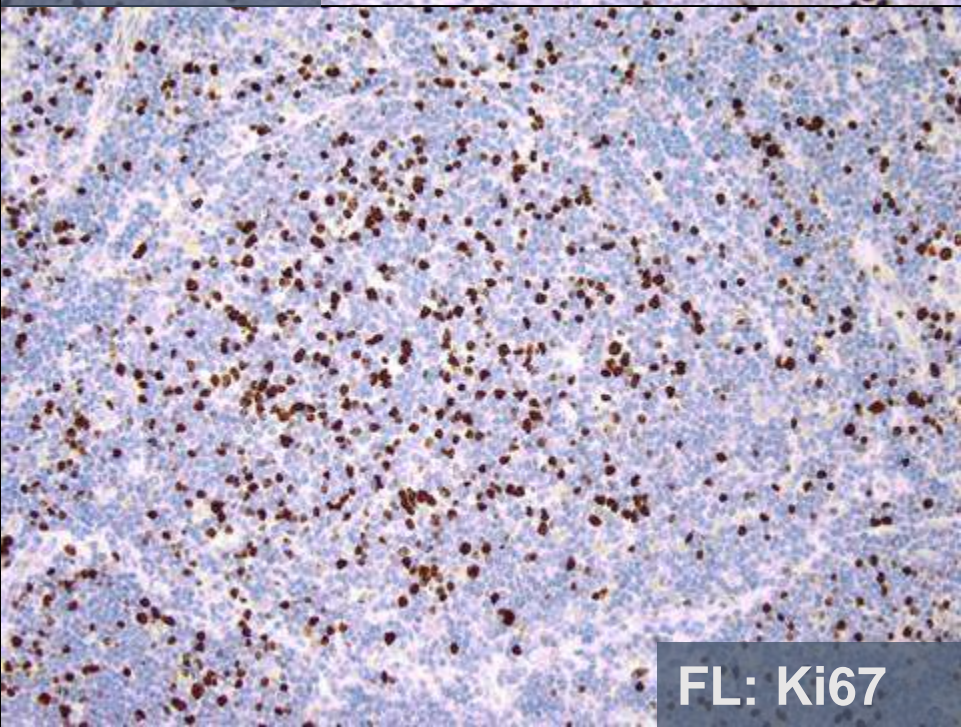
**Follicular hyperplasia: H&E**



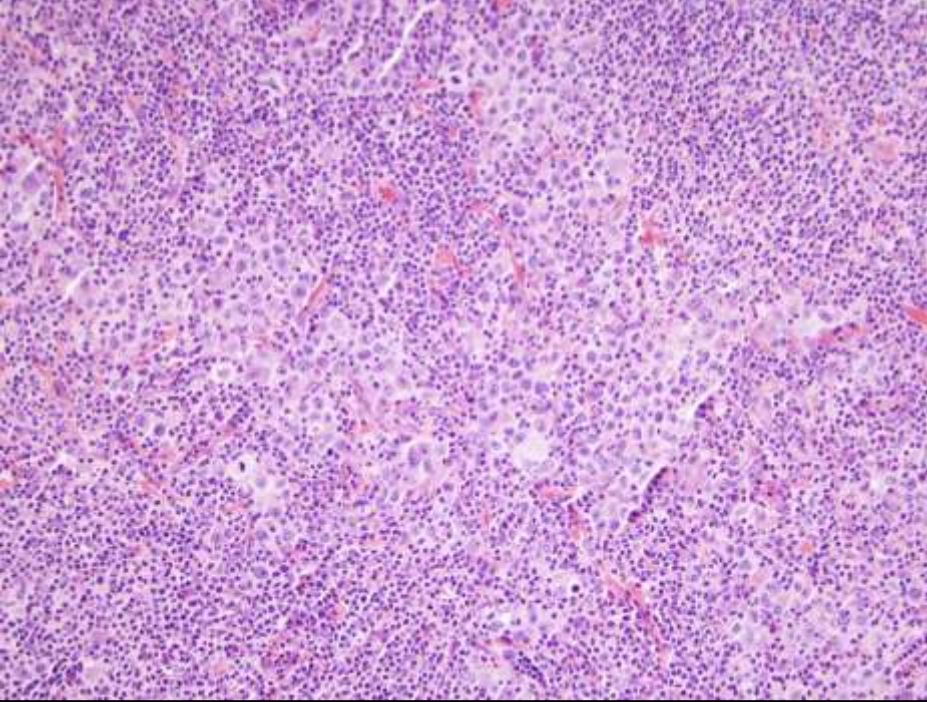
**Follicular lymphoma: H&E**



**FH: Ki67**



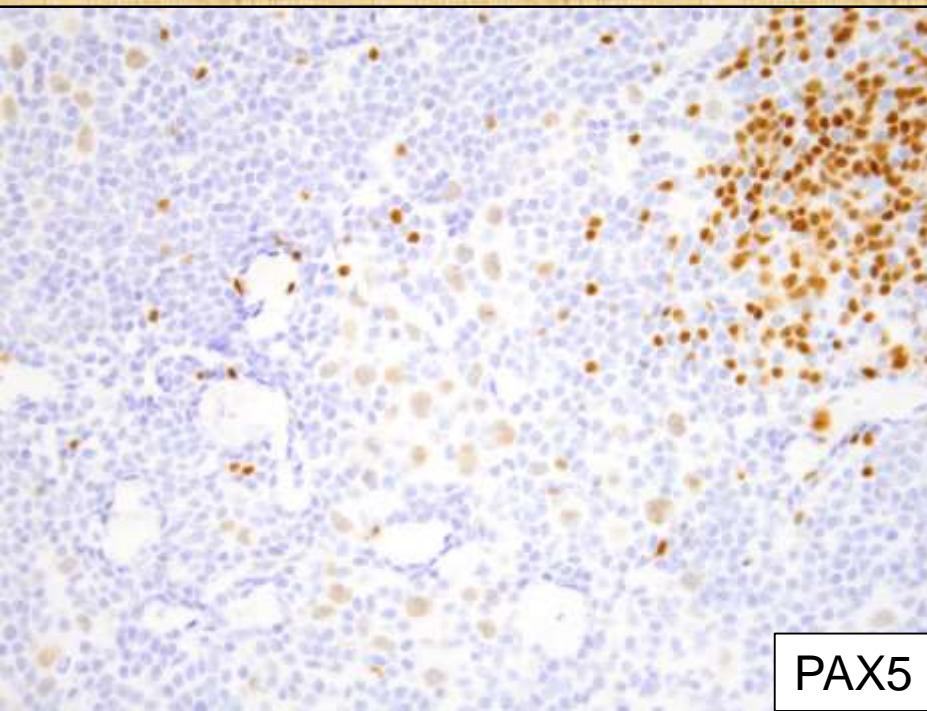
**FL: Ki67**



## Case 2

22 year old female presents with isolated neck lymphadenopathy for 2 months. She has had intermittent fevers and drenching night sweats for 3 weeks.

Q. Can a confident diagnosis be made based on the H&E stain results and the results of the PAX5 stain (shown)?



A. Yes.

B. Impossible.

C. Results should be supported by additional IHC stains.

# Hodgkin Lymphoma Approach

When do I do it?

- Polymorphous background with scattered large abnormal cells
- Bands of nodal fibrosis (e.g. nodular sclerosis)
- Scattered very large cells/any background
- Large blue nodules (NLPHL)
- Mediastinal biopsies with any of above
- Clinical: young/previous history

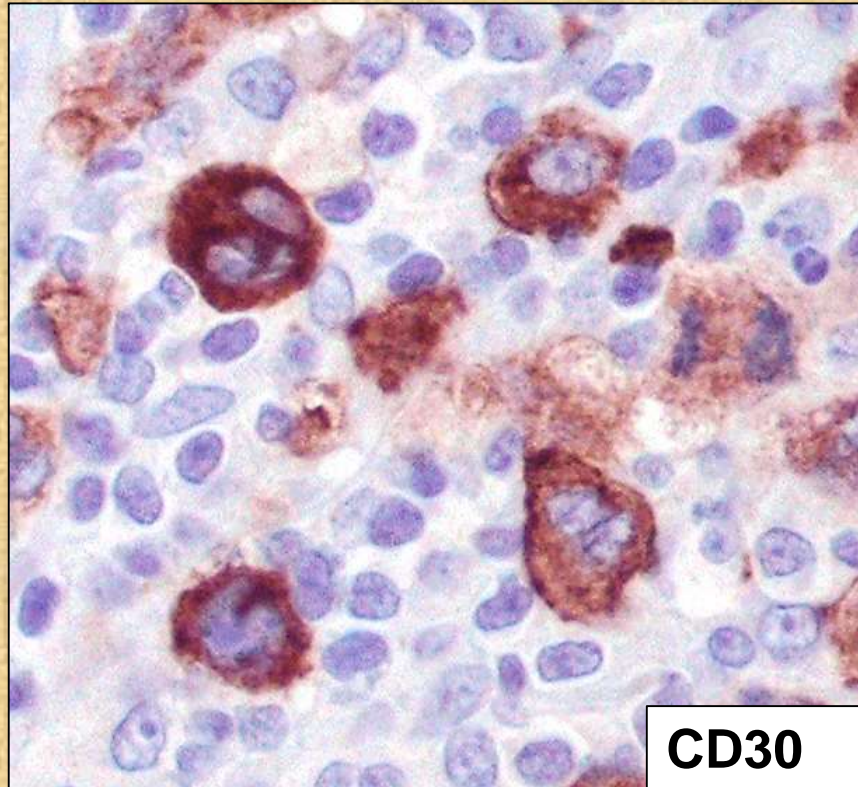
• Differential Diagnosis

- Hodgkin lymphoma
  - Classic Hodgkin lymphoma
  - Nodular lymphocyte predominant lymphoma
- T cell/histiocyte-rich large B cell lymphoma
- Reactive processes
  - Immunoblasts (transformed benign large lymphocytes)
  - Progressively transformed germinal centers (**PTGC**)

# Hodgkin Lymphoma Approach

What do I do?

- CD3
- CD20
- CD15
- CD30
- PAX5
- EBER



# Things necessary to diagnose Classic Hodgkin lymphoma

- ✓ Morphology **REQUIRED**
- ✓ CD30 positivity **REQUIRED**
- Weak staining for PAX5 **USUAL**
- ☐ CD15 positivity **SOMETIMES**
- ✓ Negative for CD45 **REQUIRED**
- Negative or weak/variable staining for CD20 **USUAL**



# Additional stains to support a diagnosis of classical Hodgkin lymphoma versus other:

## American Registry of Pathology Expert Opinions: Immunohistochemical evaluation of classic Hodgkin lymphoma

Dennis P. O'Malley<sup>a,\*</sup>, Ahmet Dogan<sup>b</sup>, Yuri Fedoriw<sup>c</sup>, L. Jeffrey Medeiros<sup>d</sup>, Chi Young Ok<sup>d</sup>, Mohamed E. Salama<sup>e</sup>

**Table 2**

Summary of immunohistochemical evaluation and expected results in classic Hodgkin lymphoma versus important differential diagnoses.

Evaluation	Stains (expected results in CHL)	Comments
Initial evaluation	CD15 (+), CD30 (+), PAX5 (+, weak-moderate intensity), CD20 (– or weak-variable), CD3 (negative)	
Versus DLBCL/TCHRLBCL	CD45 (–), OCT2 (–), BOB1 (–), CD79a (–), MUM1 (+)	
Versus PMLBCL	CD23 (–, very rarely weak and variable), CD45 (–), P63 (–), CD79a (–)	EBER and CD15 provide high specificity for CHL compared to PMLBCL
Versus ALCL	ALK (–), CD45 (–), pan T cell antigen* (–), cytotoxic markers* (–)	(Pan T: (CD2, CD5, CD7, CD43); cytotoxic markers (perforin, granzyme, TIA-1)
Versus PTCL/AITL	Pan T cell antigen (–), CD4 (–), CD8 (–), EBV (+ in 40%), FDC marker (–)	FDC markers (CD21, CD23, CD35, D2-40)
Versus NLPHL	CD21/CD23* (–), OCT2 (–/+), PD1* (*), EBV (–)	* Evaluation of FDC networks and composition of nodules, which may be present in LR-CHL as well as NLPHL

# Distinguishing Classical Hodgkin Lymphoma, Gray Zone Lymphoma, and Large B-cell Lymphoma: A Proposed Scoring System

*Dennis P. O'Malley, MD,\*† Yuri Fedoriw, MD,‡ and Lawrence M. Weiss, MD\**

**TABLE 1.** Immunohistochemical Scoring System to Distinguish Classical Hodgkin Lymphoma From B-cell Lymphoma

	Negative	Weak or Focal	Strong
CD15	0	+1	+1
CD30*	0	0	0
CD45	+1	-1	-1
CD20	+1	+1	-1
PAX5	0	+1	-1
CD79a	0	-1	-1
MUM1	-1	0	0
EBER	0	+1	+1
	Negative/ Negative	Positive/Negative or Negative/Positive	Positive/ Positive
OCT-2/ BOB.1	+1	+1	-1
	Maximum score for Hodgkin-like = +6		
	Minimum score for B cell-like = -6		

\*CD30 positivity has no results, as no staining for CD30 would be unlikely to be considered in this differential diagnosis.

+1 score indicates a finding favoring classical Hodgkin lymphoma; -1 score, a finding favoring B-cell lymphoma. A score of 0 indicates a finding that is either equivocal or not strongly supportive of either diagnosis.

		<del>CD30</del>	
		CD15	➔
	➔	CD45	
	➔	CD20	
	➔	PAX5 (strong)	
	➔	CD79a	
	➔	MUM1(-)	
		EBER	➔
	➔	OCT2 & BOB1	
<b>B</b>			<b>C</b>
<b>C</b>			<b>H</b>
<b>L</b>			<b>L</b>

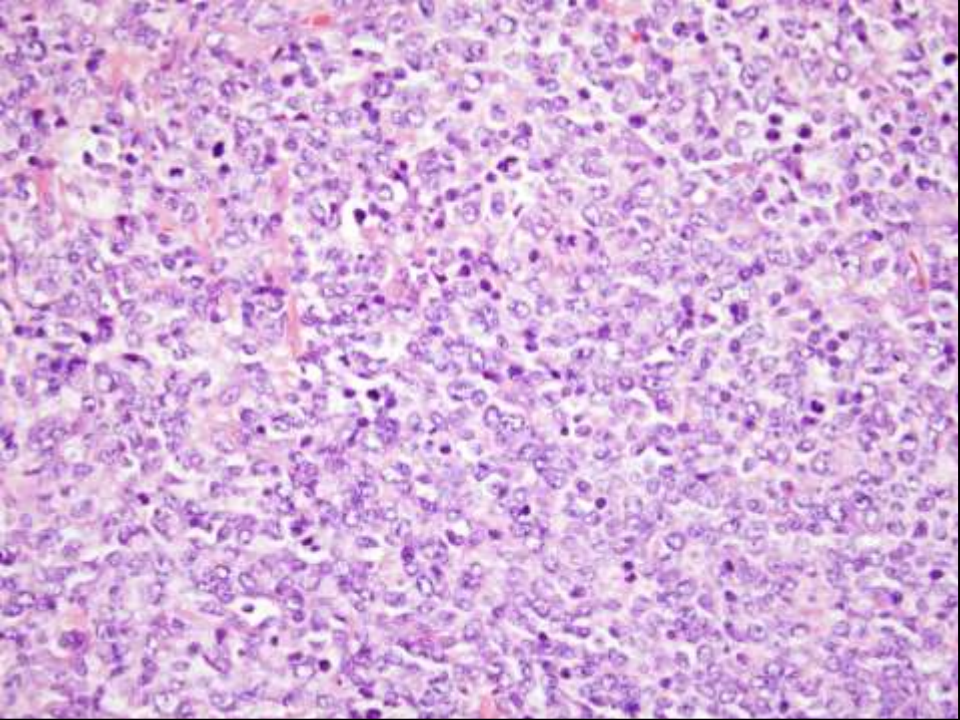
**TABLE 2. Reported Frequency of Immunohistochemical Markers in Classical Hodgkin Lymphoma and Diffuse Large B-cell Lymphoma**

Marker	CHL	DLBCL	PMLBCL
CD15	75%-90% <sup>10-12</sup>	0% Est.	0% <sup>12,13</sup>
CD30	92%-100% <sup>11,12</sup>	21% <sup>14</sup>	19%-86% <sup>12,13</sup>
CD45	14% <sup>15</sup>	100% Est.	100% <sup>13</sup>
CD20	23%-30% <sup>10-12</sup>	97%-100% <sup>10,14</sup>	100% <sup>12,13</sup>
PAX5	90% <sup>10,11*</sup>	93%-100% <sup>10,14</sup>	100% <sup>13</sup>
CD79a	6%-11% <sup>10,12,16</sup>	86%-100% <sup>10,14</sup>	89%-100% <sup>12,13</sup>
OCT-2	13%-33% <sup>10-12</sup>	94%-100% <sup>10</sup>	97%-100% <sup>12,13</sup>
BOB.1	15%-53% <sup>10,11,16</sup>	96%-100% <sup>10</sup>	100% <sup>12,13</sup>
MUM1	92%-100% <sup>11,16</sup>	35%-65% <sup>14</sup>	75% <sup>13</sup>
EBV/EBER	32%-36% <sup>11,17†</sup>	4% <sup>14</sup>	NR

\*Positivity does not account for difference of intensity seen in Hodgkin cells versus B cells.

†Prevalence in Europe and North America from Lee et al.<sup>17</sup>

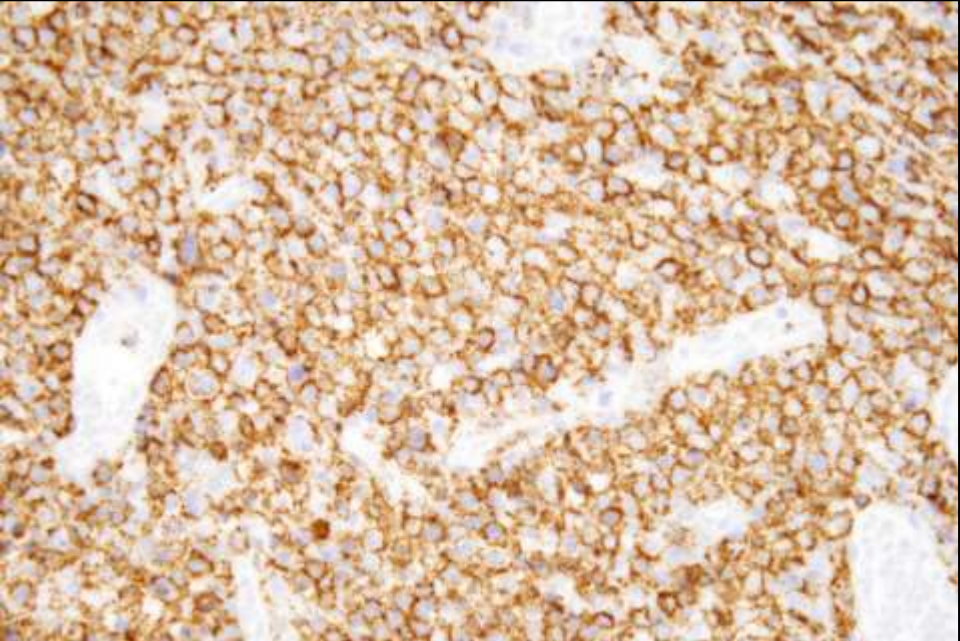
CHL indicates classical Hodgkin lymphoma; DLBCL, diffuse large B-cell lymphoma; EBV/EBER, Epstein-Barr virus/Epstein-Barr early RNA; Est., estimated; NR, not reported; PMLBCL, primary mediastinal large B-cell lymphoma.



### Case 3

68 year old female presents with a rapidly growing mass in her thyroid. An FNA is indeterminate. A thyroidectomy is performed and a tumor (4.5 cm in greatest diameter is identified).

Q. Which of the following additional stain(s) may change therapy?



CD20

A. CD30

B. CD5

C. MYC and BCL2

# Large B cell Lymphoma Approach

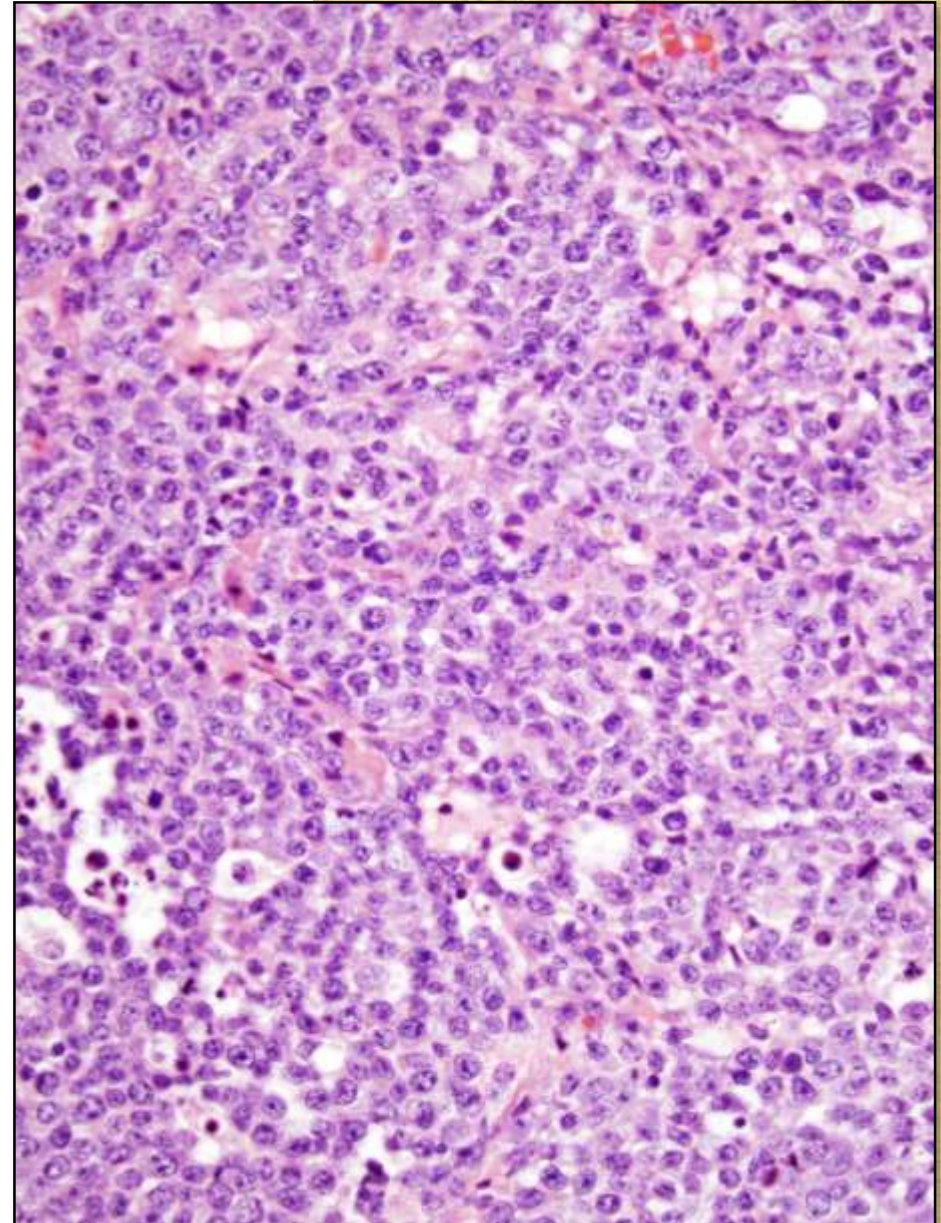
## When do I do it?

- (NEW DIAGNOSIS)
- Diffuse sheets of large hematopoietic cells
- Diffuse sheets of intermediate sized hematopoietic cells

# Large B cell Lymphoma Approach

## What do I do?

- CD3
- CD20
- CD5, CD10
- Cyclin D1
- BCL2, BCL6
- CD30
- MUM1
- Ki67
- EBER
- CMYC
- p53



# Large B cell Lymphoma Approach

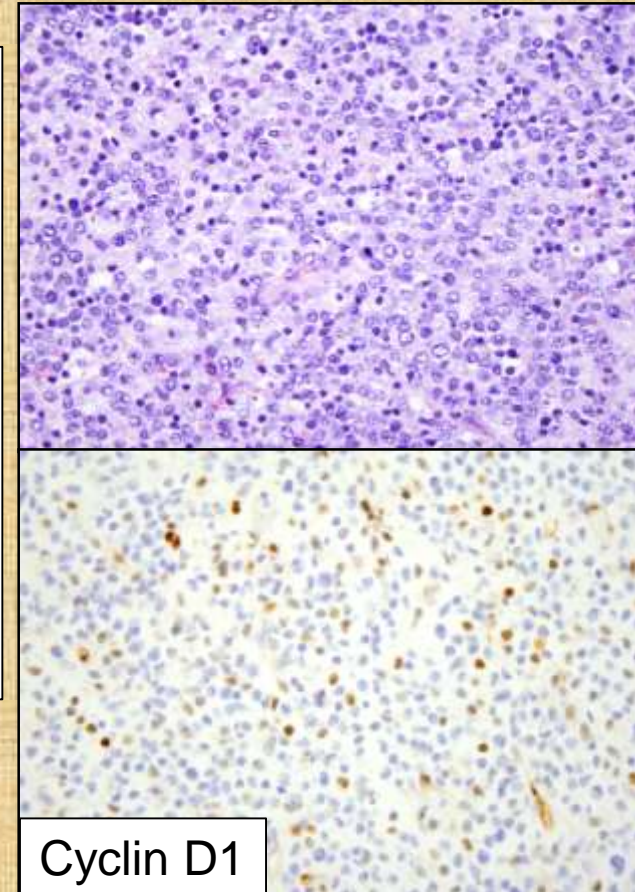
## What do I do?

- CD3
- CD20
- **CD5**, CD10
- **Cyclin D1**
- BCL2, BCL6
- CD30
- MUM1
- Ki67
- EBER
- CMYC
- p53

CD5 positive DLBCL, associated with a worse prognosis

Evaluate for possible *blastoid mantle cell lymphoma*

Subset of DLBCL have partial positivity for cyclin D1, with no specific prognostic implications



# Diffuse Large B cell Lymphoma

**GERMINAL  
CENTER**

**=**

**GOOD**

**NON-GERMINAL  
CENTER or ABC**

**=**

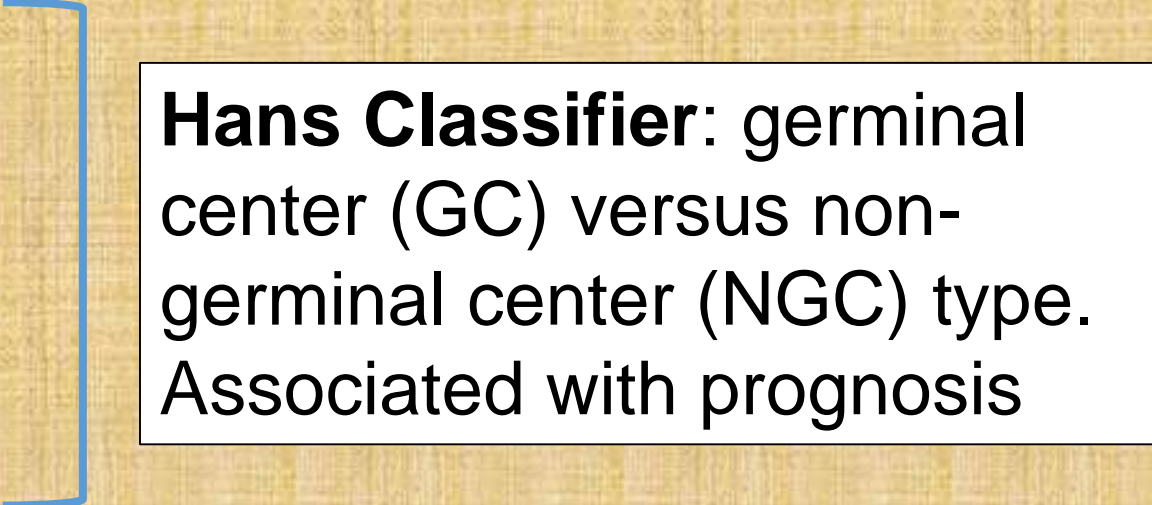
**BAD**



# Large B cell Lymphoma Approach

## What do I do?

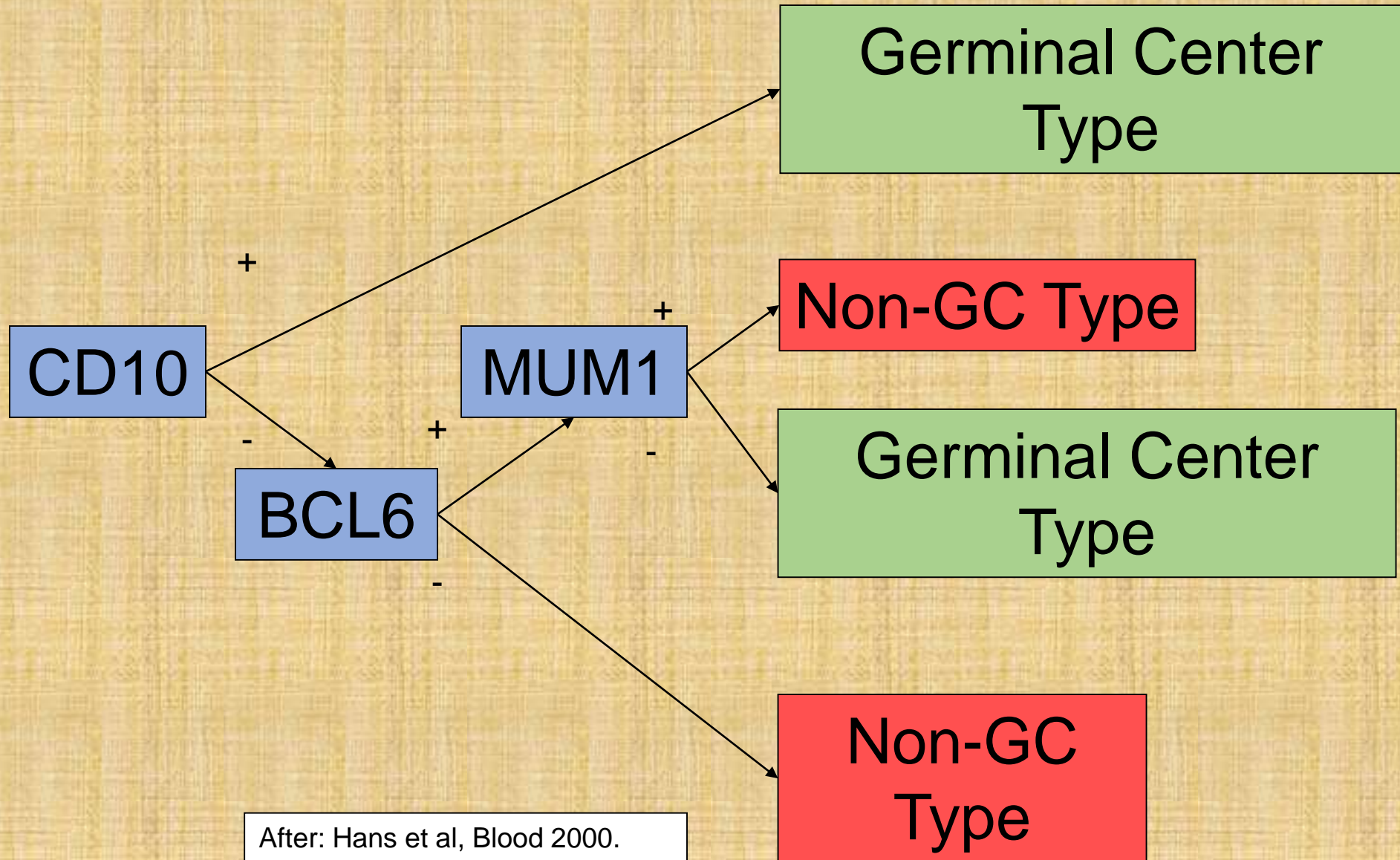
- CD3
- CD20
- CD5, **CD10**
- Cyclin D1
- BCL2, **BCL6**
- CD30
- **MUM1**
- Ki67
- EBER
- CMYC
- p53



**Hans Classifier:** germinal center (GC) versus non-germinal center (NGC) type. Associated with prognosis

# HANS CLASSIFIER

Prognosis in Diffuse  
Large B cell Lymphoma



After: Hans et al, Blood 2000.

# EDITORIAL COMMENT

- We are approaching 20 years of cell of origin (COO) analysis in DLBCL
- Recent publications have proposed molecular classifiers with 5+ types of DLBCL
- We currently have not used COO in a consistent way to affect outcomes

# Large B cell Lymphoma Approach

## What do I do?

- CD3
- CD20
- CD5, CD10
- Cyclin D1
- BCL2, BCL6
- CD30
- MUM1
- **Ki67**
- EBER
- CMYC
- p53

Proliferation index, as assessed by Ki67 can help subclassify some types, and has a weak association with prognosis

Patterns can help identify cell types and help in differential diagnosis

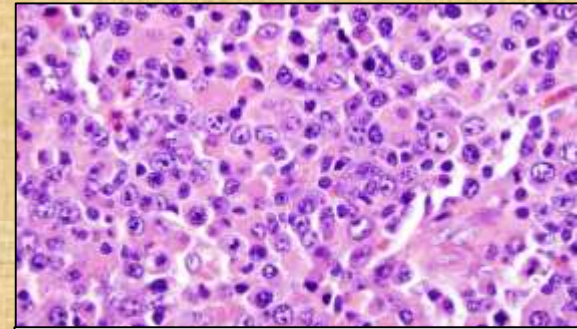
# Large B cell Lymphoma Approach

## What do I do?

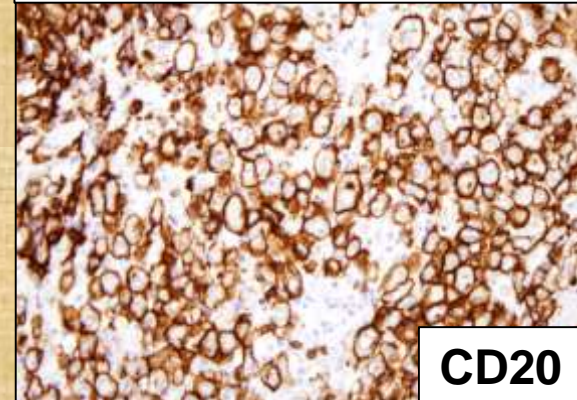
- CD3
- CD20
- CD5, CD10
- Cyclin D1
- BCL2, BCL6
- CD30
- MUM1
- Ki67
- **EBER**
- CMYC
- p53

Positivity for EBV (by in situ staining or EBER) identifies several special subtypes of DLBCL. In general these are associated with a worse prognosis. These include:

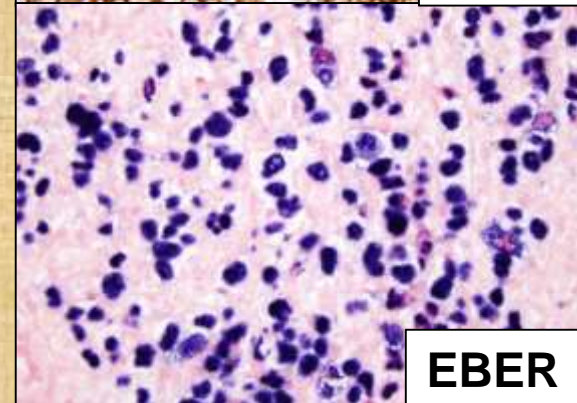
- EBV positive DLBCL
- DLBCL associated with chronic inflammation
- Plasmablastic lymphoma
- Primary effusion lymphoma
- Lymphomatoid granulomatosis



EBV POSITIVE DLBCL



CD20



EBER

# Large B cell Lymphoma Approach

## What do I do?

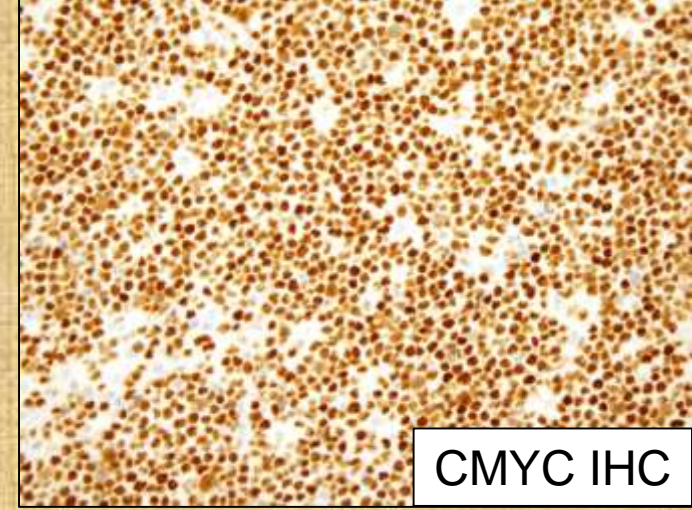
- CD3
- CD20
- CD5, CD10
- Cyclin D1
- **BCL2**, BCL6
- CD30
- MUM1
- Ki67
- EBER
- **MYC**
- p53

Positivity for MYC immunohistochemistry is seen in all cases of DLBCL

**Positivity in large percentage of cells for MYC IHC, correlates well with MYC gene abnormalities**

This may mean either *MYC* gene *translocations* OR *MYC* gene *amplifications*

These studies also suggest that high MYC with BCL2 expression by IHC are associated with a poor prognosis (double expressor)

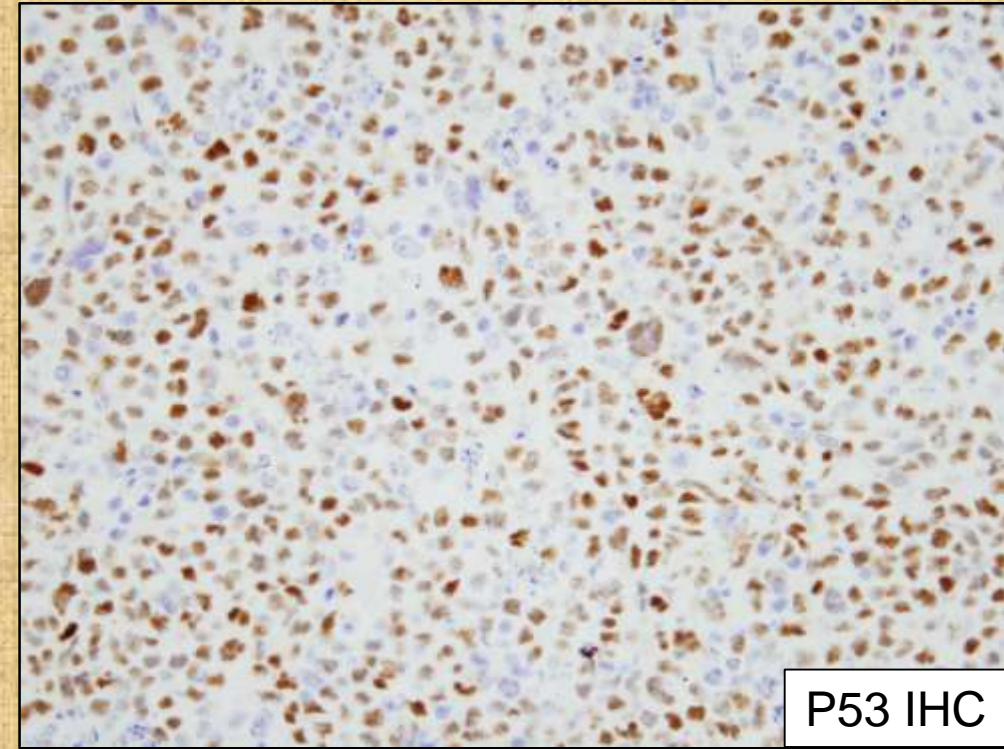


CMYC IHC

# Large B cell Lymphoma Approach

## What do I do?

- CD3
- CD20
- CD5, CD10
- Cyclin D1
- BCL2, BCL6
- CD30
- MUM1
- Ki67
- EBER
- CMYC
- **p53**



P53 overexpression in lymphoma is associated with a poor prognosis.

Generally, any expression over 20% is associated with a poor prognosis

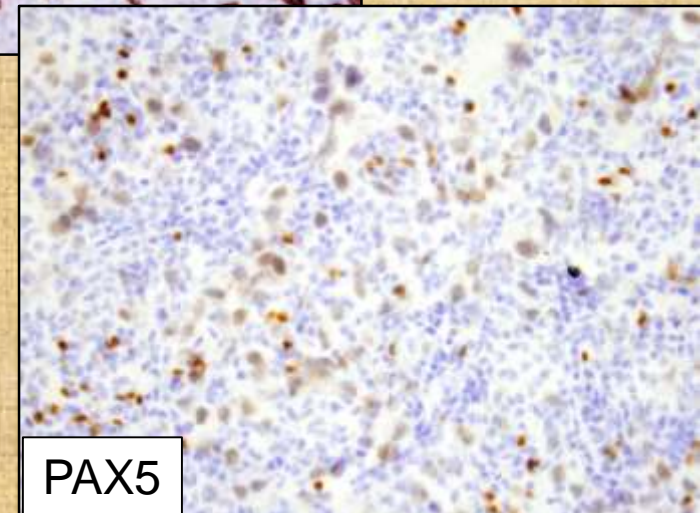
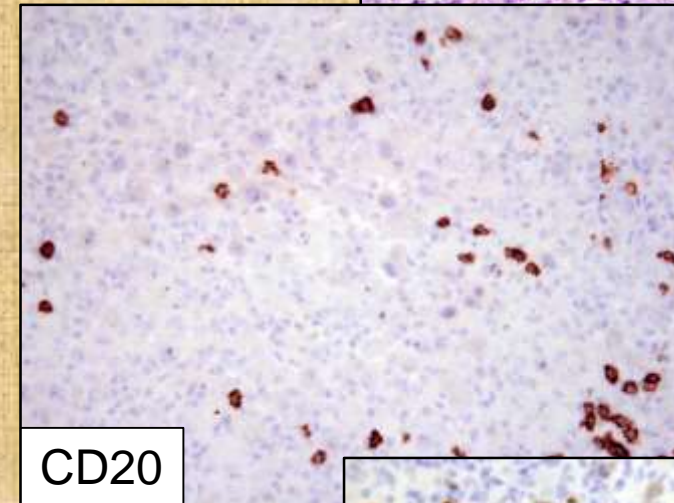
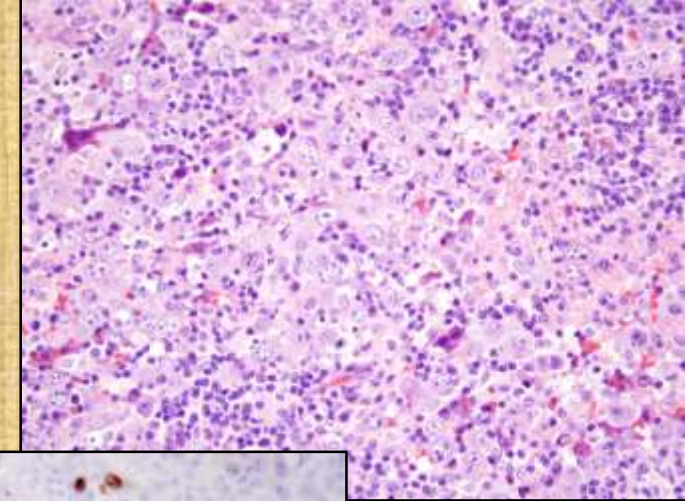
Overexpression is not always associated with *TP53* gene abnormality

# AN ASIDE...

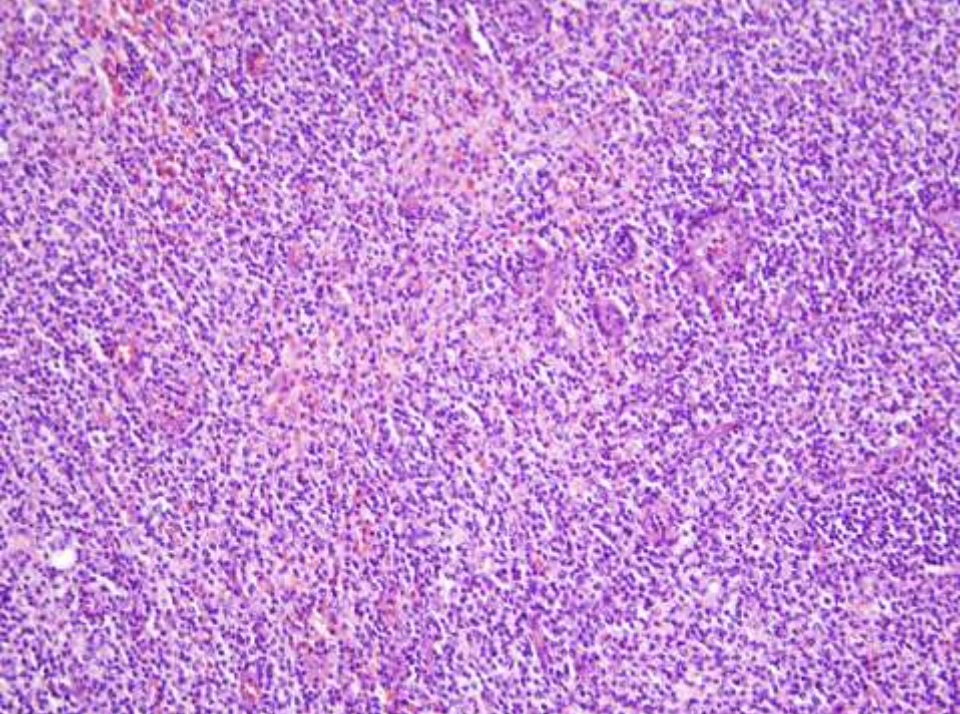
## TO PAX5 OR NOT TO PAX5?

- Should a back-up B cell marker be performed in all cases (up-front)?
  - In my opinion, **NO**
  - 98%+ of B cell lymphomas express CD20 initially
  - **HOWEVER**, if there is any history of previous lymphoma, or if history is unclear, (or possible issues of TAT), then I perform a PAX5\*

\*You could also use CD79a, CD19 or CD22 in most circumstances. I prefer PAX5 because it is robust nuclear staining



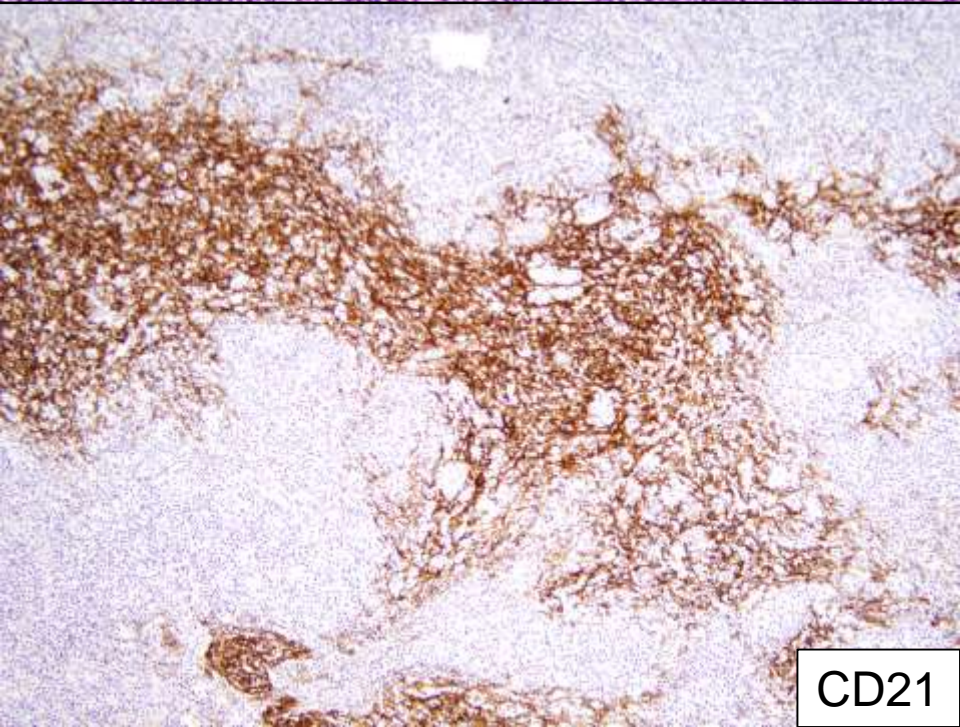




## Case 4

82 year old male presents fevers and weight loss of 30 pounds over past 6 months. On evaluation, diffuse adenopathy is identified. An excisional biopsy of an enlarged cervical node is performed.

Q. Based on the H&E stain and results of CD21 stain, what additional studies would best confirm a diagnosis of angioimmunoblastic T cell lymphoma?



A. CD30, ALK1, TIA1

B. PD1, EBER, BCL6, CD10

C. CD4, CD8, CD2, CD5, CD7

# T cell lymphoma Approach

- **When do I do it?**

- When background suggests T cell lymphoma
  - Not always easy to describe
- Polymorphous cellular background with significant cytologic atypia
- Small or polymorphous lymphocytes with increased
  - Vasculature
  - Histiocytes
  - Eosinophils
- Increased numbers of lymphocytes with pale cytoplasm
- Sheets or intrasinusoidal large/anaplastic lymphoid cells

# T cell Lymphoma

- **What do I do?**

- *The kitchen sink!*
- CD3, CD2, CD4, CD5, CD7, CD8, CD56
- CD30
- ALK1, P63
- BCL2
- CD21, PD1, BCL6, CD10, CXCL13, ICOS
- Ki67
- EBER
- TCR beta F1, TCR delta
- TIA1, perforin, granzyme B

# T cell Lymphoma

- What do I do?
  - CD3, CD2, CD4, CD5, CD7, CD8, CD56
  - CD30
  - ALK1, P63
  - BCL2
  - CD21, PD1, BCL6, CD10, CXCL13, ICOS
  - Ki67
  - EBER
  - TCR beta F1, TCR delta
  - TIA1, perforin, granzyme B

Pan T cell antigens: Loss would indicate an abnormal T cell population  
CD7 loss can be seen in some reactive processes  
Overexpression of CD56 is usually abnormal

# T cell Lymphoma

## • What do I do?

- CD3, CD2, **CD4**, CD5, CD7, **CD8**, CD45, CD45RO, CD45RA, CD45RB, CD45RC, CD45RD, CD45RE, CD45RF, CD45RG, CD45RH, CD45RI, CD45RJ, CD45RK, CD45RL, CD45RM, CD45RN, CD45RO, CD45RP, CD45RQ, CD45RS, CD45RT, CD45RU, CD45RV, CD45RW, CD45RX, CD45RY, CD45RZ, CD45RA, CD45RB, CD45RC, CD45RD, CD45RE, CD45RF, CD45RG, CD45RH, CD45RI, CD45RJ, CD45RK, CD45RL, CD45RM, CD45RN, CD45RO, CD45RP, CD45RQ, CD45RS, CD45RT, CD45RU, CD45RV, CD45RW, CD45RX, CD45RY, CD45RZ
- CD30
- ALK1, P63
- BCL2
- CD21, PD1, BCL6, CD10, CXCL13, CD138, CD137, CD137L, CD137R, CD137S, CD137T, CD137U, CD137V, CD137W, CD137X, CD137Y, CD137Z, CD137A, CD137B, CD137C, CD137D, CD137E, CD137F, CD137G, CD137H, CD137I, CD137J, CD137K, CD137L, CD137M, CD137N, CD137O, CD137P, CD137Q, CD137R, CD137S, CD137T, CD137U, CD137V, CD137W, CD137X, CD137Y, CD137Z
- Ki67
- EBER
- TCR beta F1, TCR delta
- TIA1, perforin, granzyme B

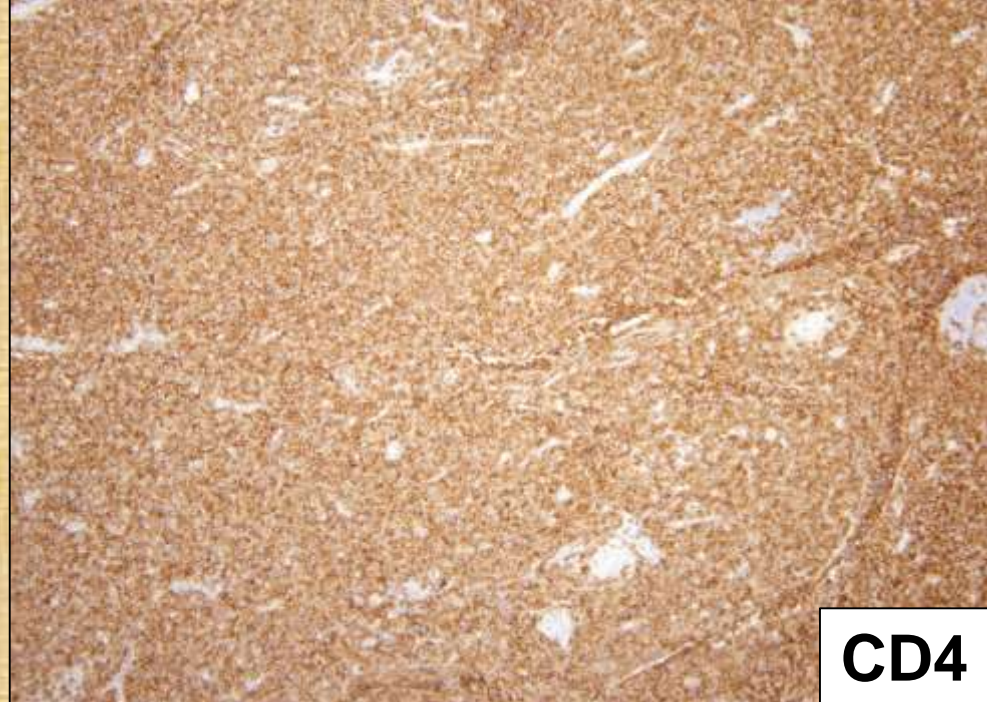
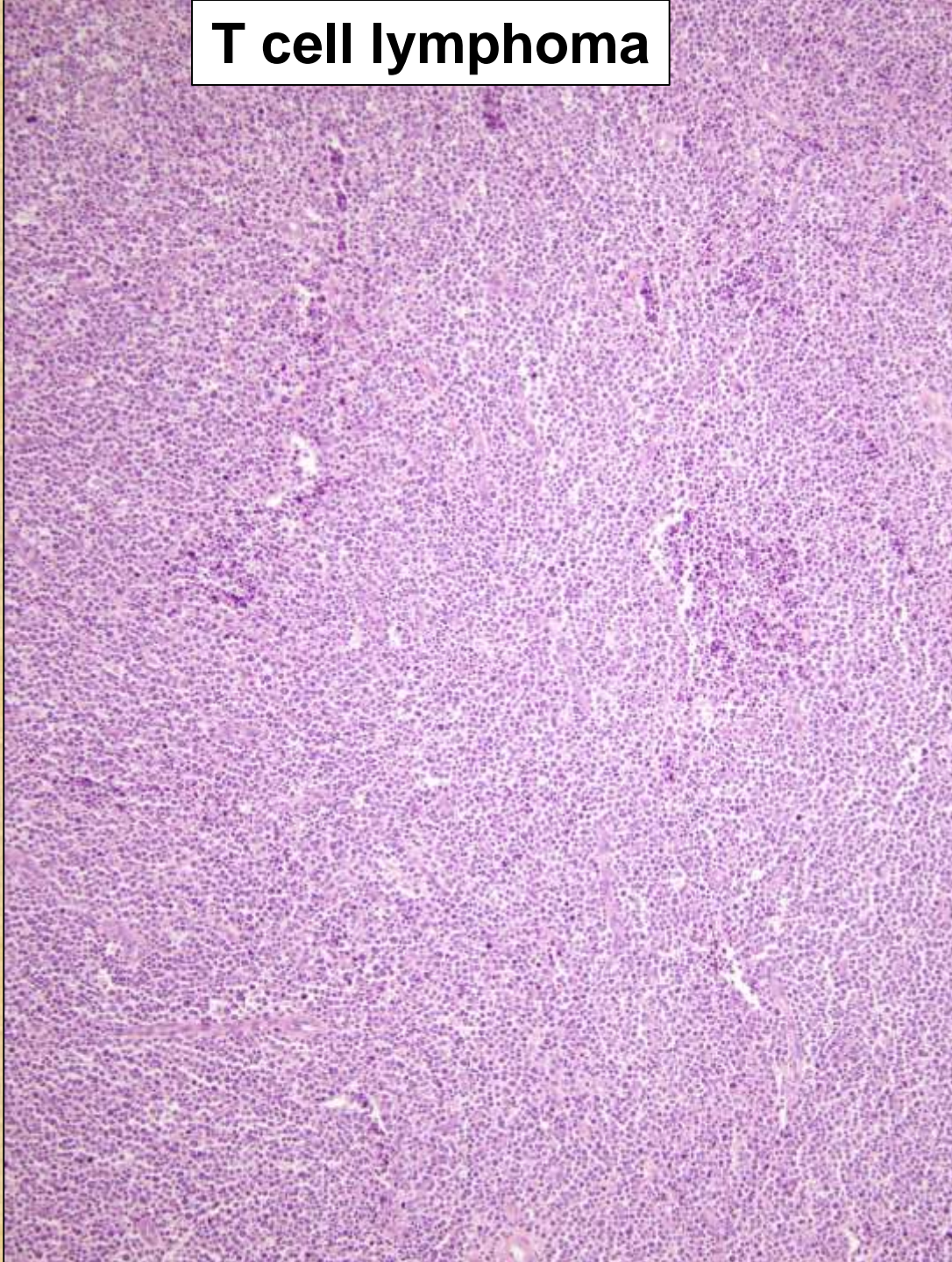
Most reactive T cell processes are a mixture of CD4 and CD8 positive T cells

When there is a strong bias of CD4 or CD8, then this is more likely T cell lymphoma

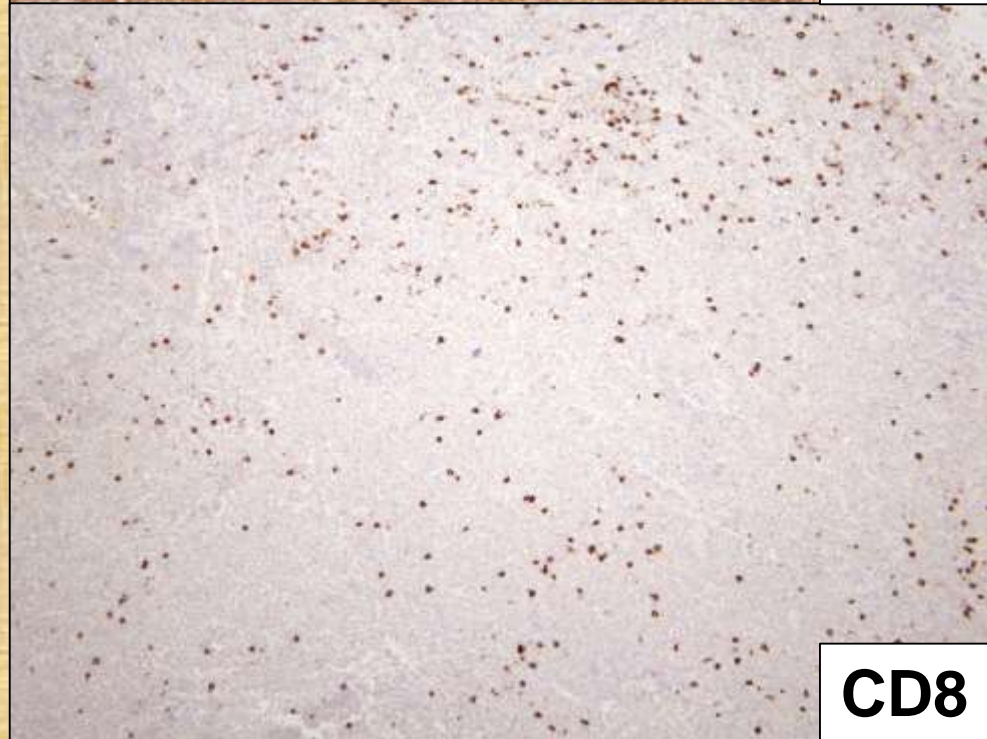
When there is coexpression of CD4/CD8 this is usually abnormal

When T cells lack CD4/CD8, this is usually abnormal

**T cell lymphoma**



**CD4**



**CD8**

# T cell Lymphoma

- What do I do?

- CD3, CD2, CD4, CD5, CD7, CD8, CD56
- **CD30**
- **ALK1, P63**
- BCL2
- CD21, PD1, BCL6, CD10, CXCL13, ICOS
- Ki67
- EBER
- TCR beta F1, TCR delta
- TIA1, perforin, granzyme B

Evaluate for anaplastic  
large cell lymphoma

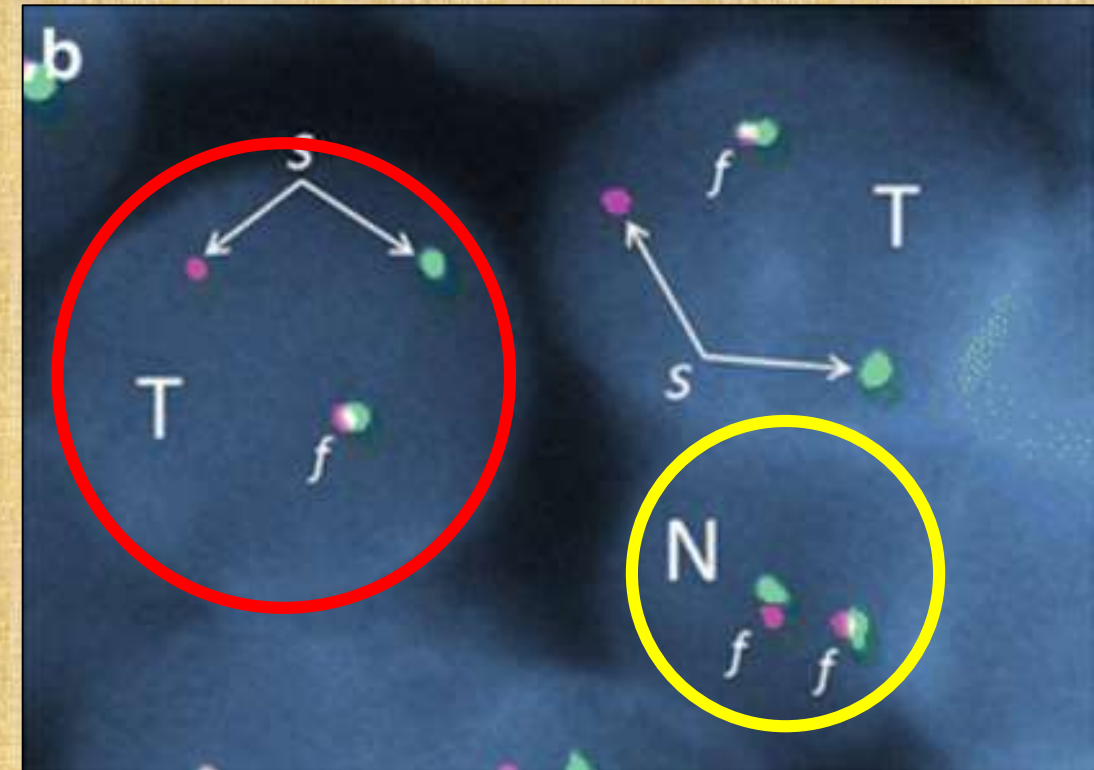
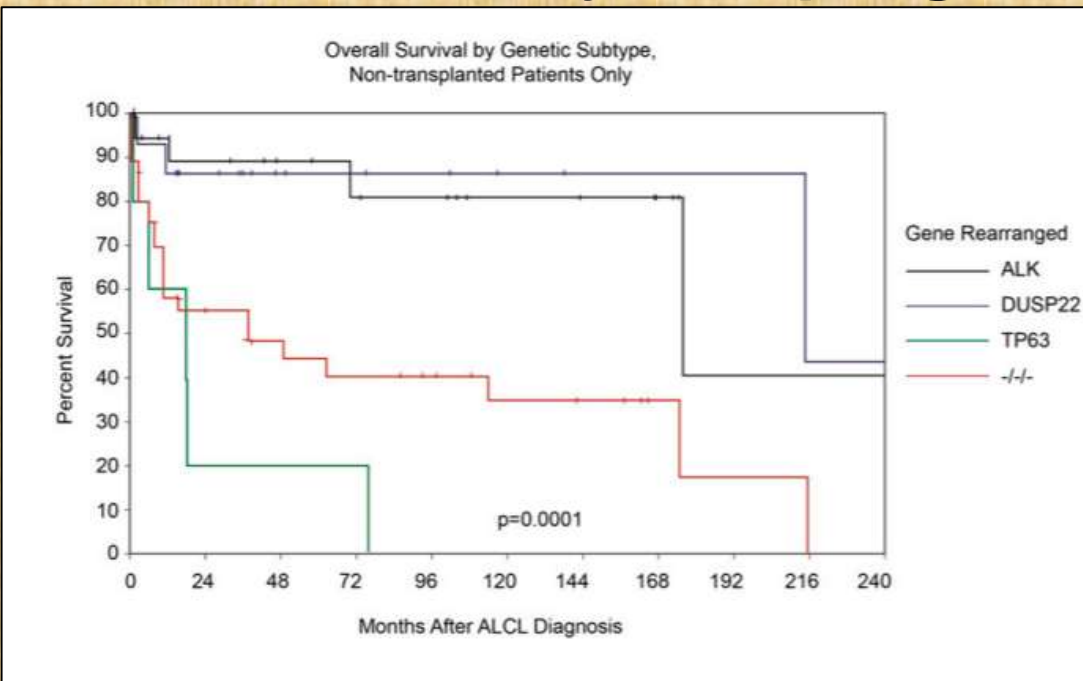
# Systemic ALCL

ALCL, ALK+: good prognosis

ALCL, *DUSP22/IRF4*: intermediate

ALCL, triple negative: **very bad prognosis**

ALCL, *TP63*: **very bad prognosis**



*DUSP22*: break-apart probe



# Practical pathology assessment of ALCL

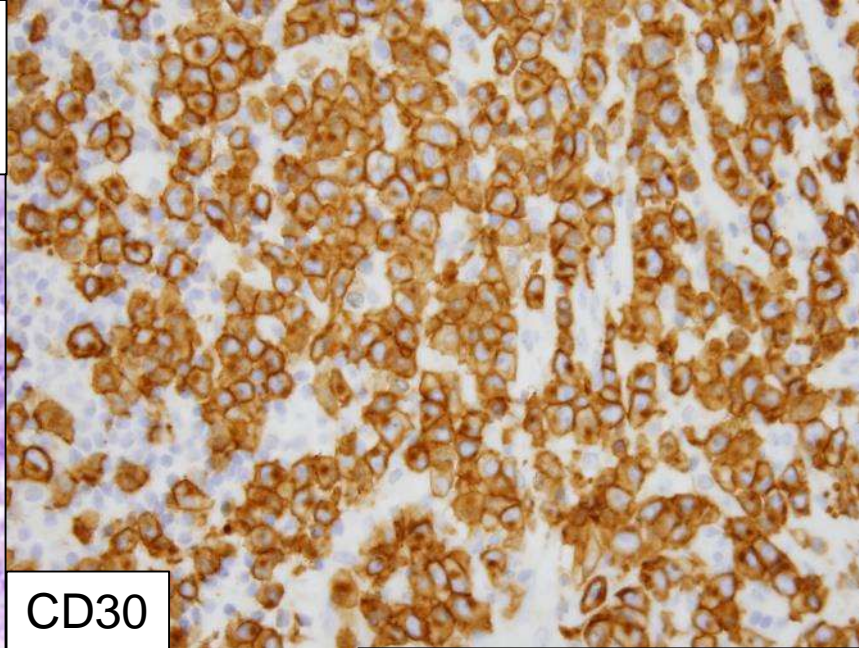
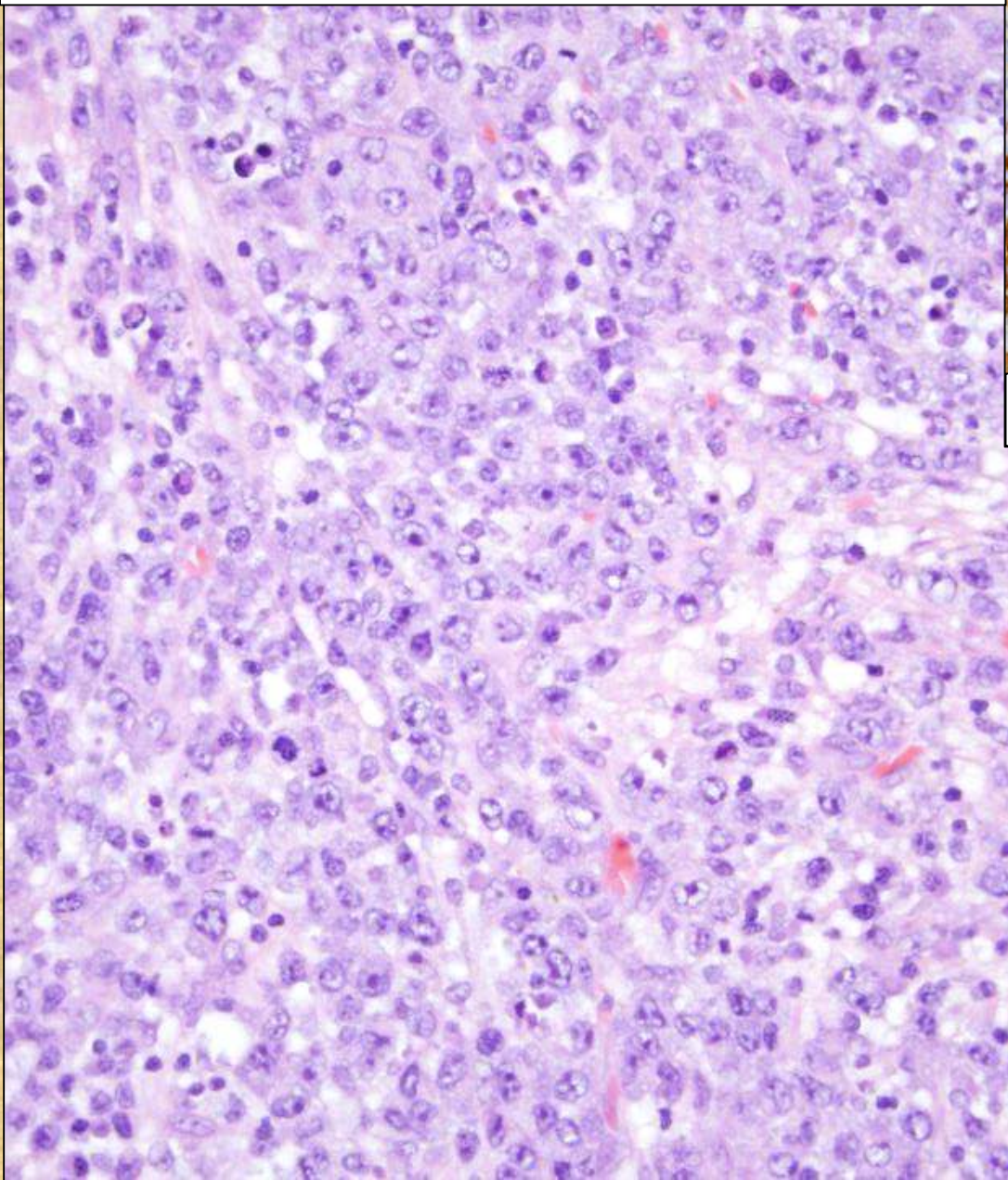
- Identify T cell lymphoma with CD30 expression (in >75% of cells, strong)
- Location/clinical:
  - Is it skin? Breast capsule?
  - Is it lymph node? Extranodal?
- If ALCL, evaluate ALK by IHC
  - If ALK+, done. S-ALCL, ALK positive
- If ALK-, (e.g. S-ALCL, ALK negative)
  - FISH for *DUSP22* (positive, good prognosis)
  - \*FISH *TP63* (positive, POOR prognosis)
  - If negative for all, then “triple negative” (poor prognosis)

**NOTICE:  
BI-ALCL IS NOW AN  
FDA REPORTABLE  
EVENT**

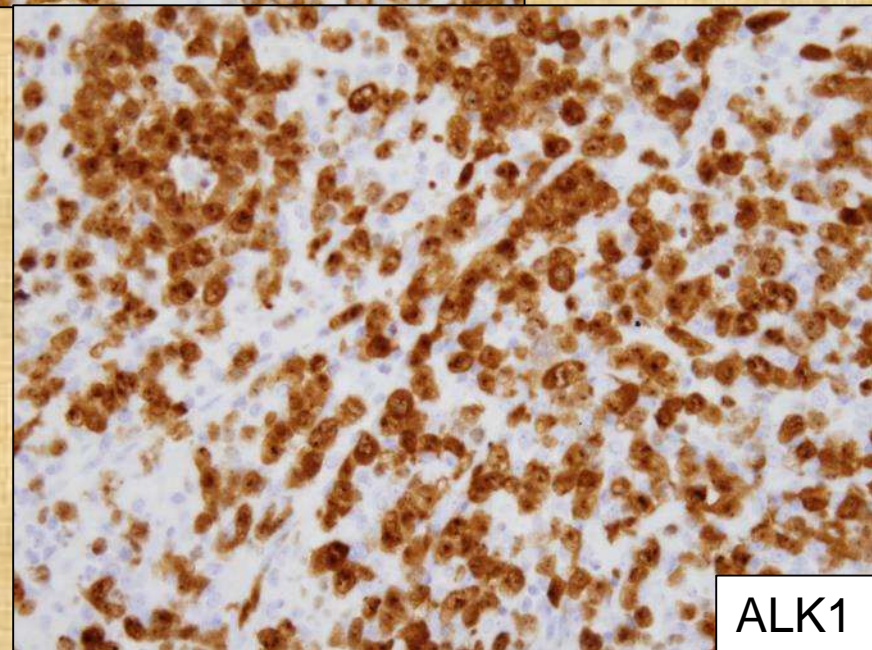
<https://www.fda.gov/MedicalDevices/Safety/LetterstoHealthCareProviders/ucm630863.htm>

\*Can screen for *TP63* by performing IHC

**Anaplastic large cell lymphoma,  
ALK+**

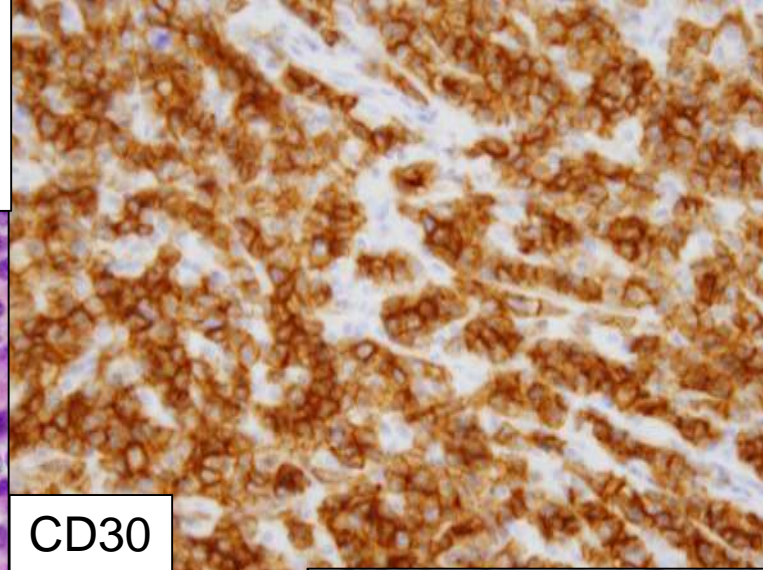
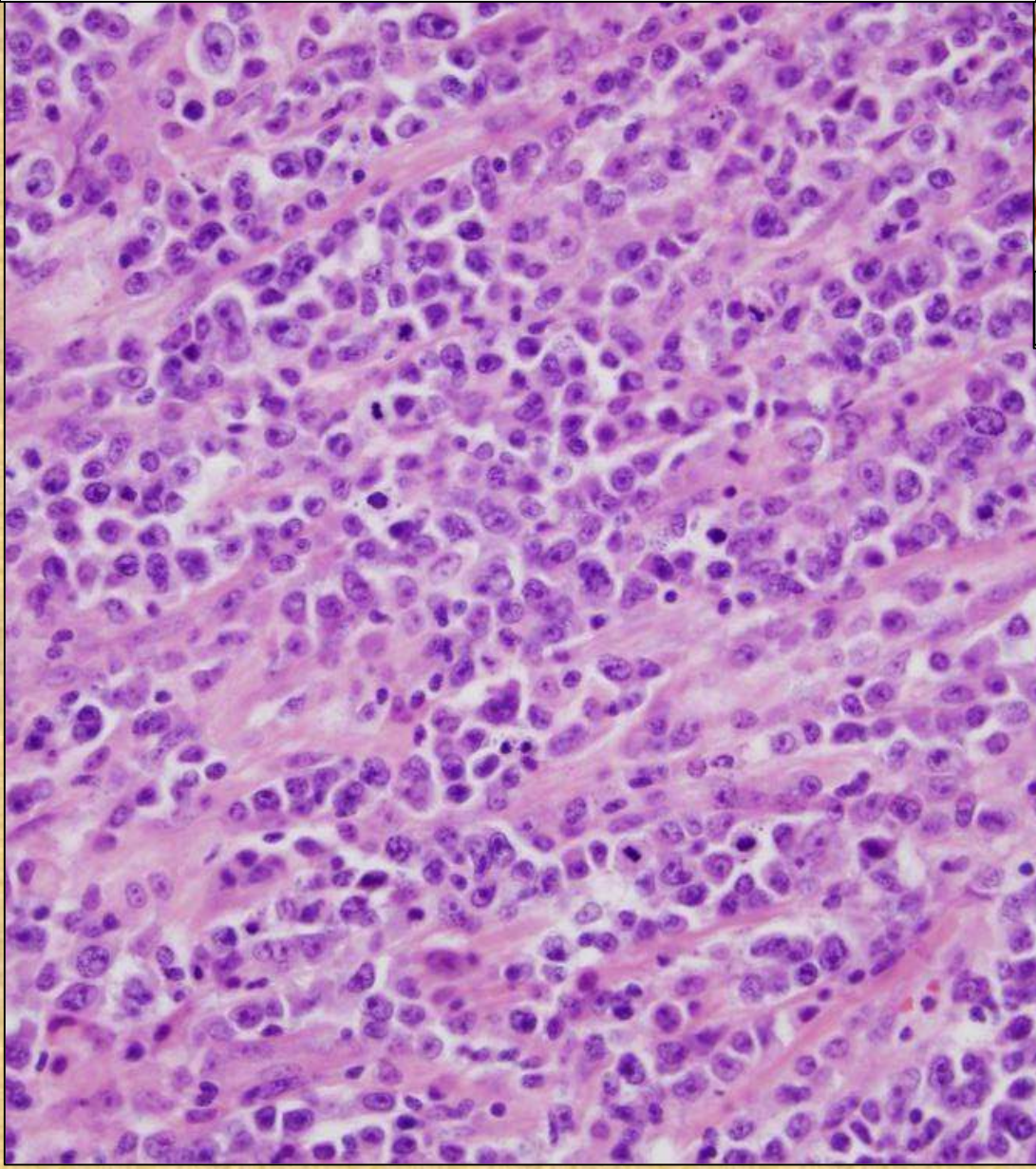


CD30

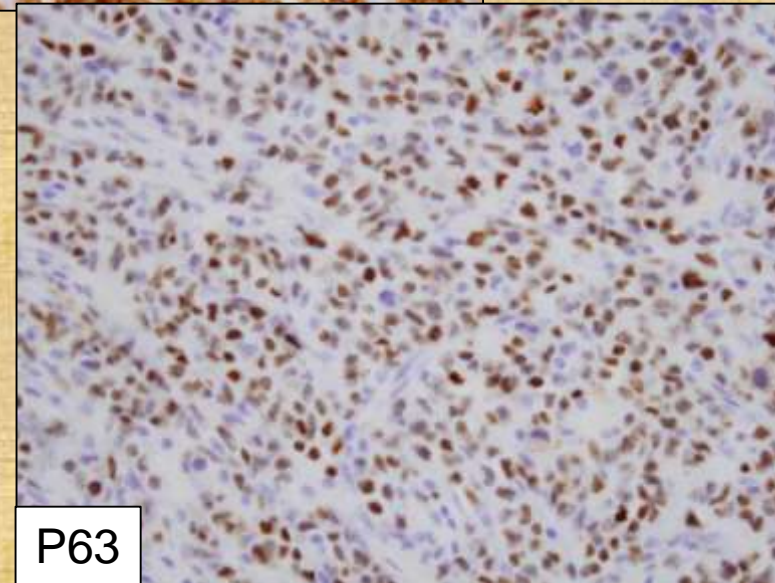


ALK1

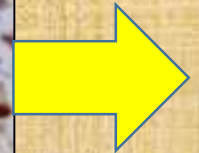
**Anaplastic large cell lymphoma,  
ALK negative  
? *TP63* translocation**



CD30



P63



*TP63*  
FISH

# T cell Lymphoma

- What do I do?

- CD3, CD2, CD4, CD5, CD7, CD8, CD56
- CD30
- ALK1, P63

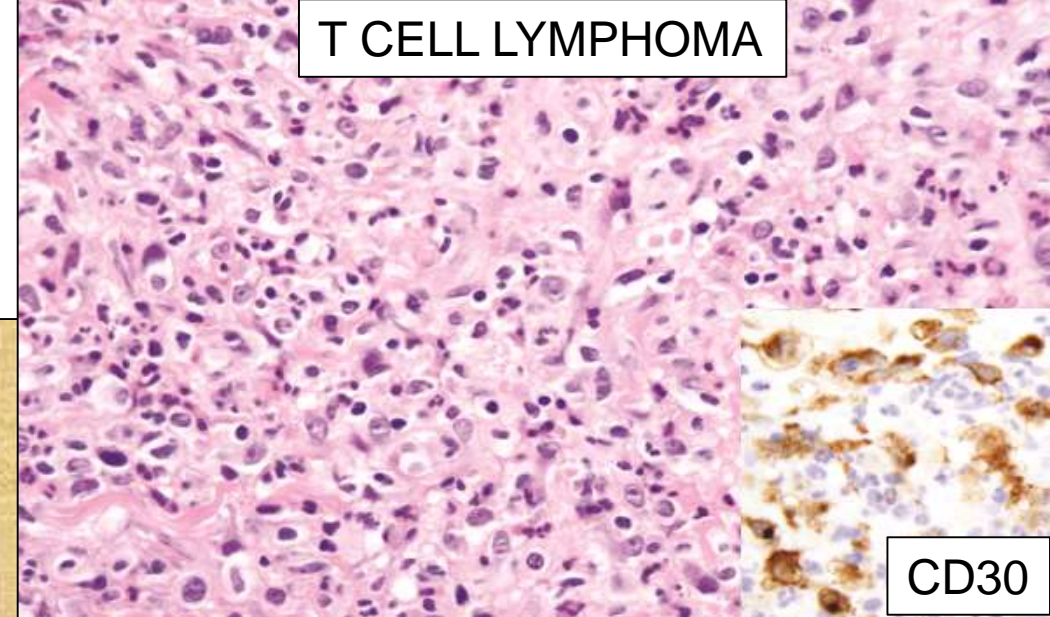
- **BCL2**

**AID IN DIAGNOSIS  
LOSS IS NOT NORMAL FOR T CELLS**

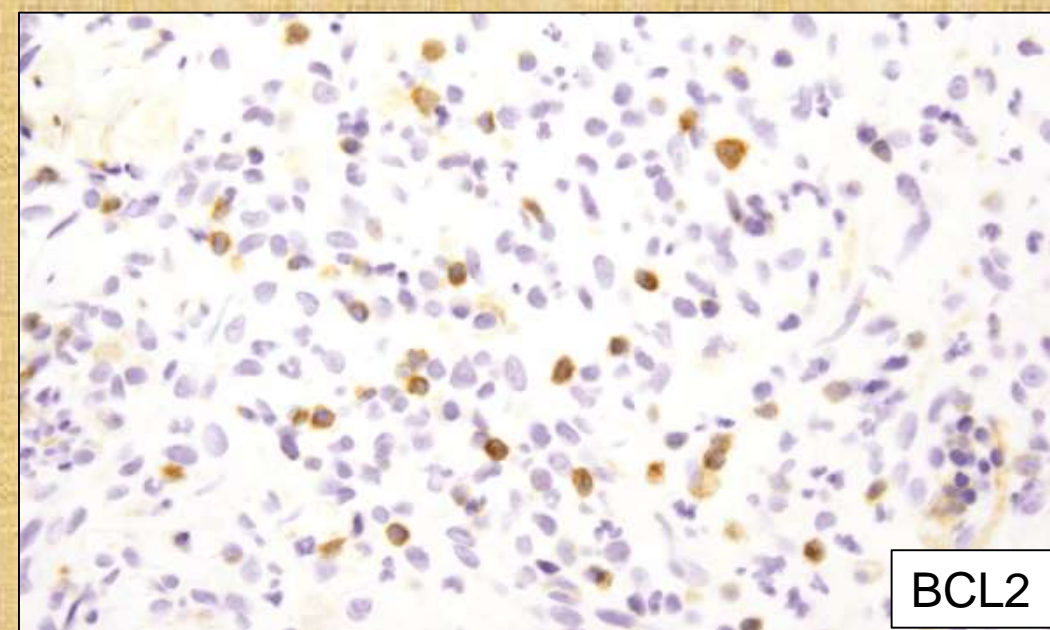
- CD21, PD1, BCL6, CD10, CXCL13, ICOS
- Ki67
- EBER
- TCR beta F1, TCR delta
- TIA1, perforin, granzyme B

# Utility of BCL2, PD1, and CD25 Immunohistochemical Expression in the Diagnosis of T-cell Lymphomas

*Dennis P. O'Malley, MD, Vladislav Chizhevsky, MD, Kate E. Grimm, MD, Anselm Hii, MD, and Lawrence M. Weiss, MD*



CD30



BCL2

**TABLE 1. Immunohistochemical Staining in T-cell Lymphomas**

Type	N	BCL-2 Negative	PD-1 Positive	CD25 Positive
AITL	21	6/21 (29%)	12/15 (80%)	7/19 (37%)
ALCL ALK <sup>+</sup>	18	15/17 (88%)	1/16 (6%)	12/17 (71%)
ALCL ALK <sup>-</sup>	32	22/32 (69%)	3/28 (11%)	19/30 (63%)
PTCL	39	16/38 (44%)	8/34 (24%)	15/36 (42%)
Other	9	1/8 (13%)	0/8 (0%)	0/8 (0%)
All cases	119	60/116 (52%)	24/101 (24%)	53/110 (48%)

AITL indicates angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large cell lymphoma; PTCL, peripheral T-cell lymphoma, unspecified.

# T cell Lymphoma

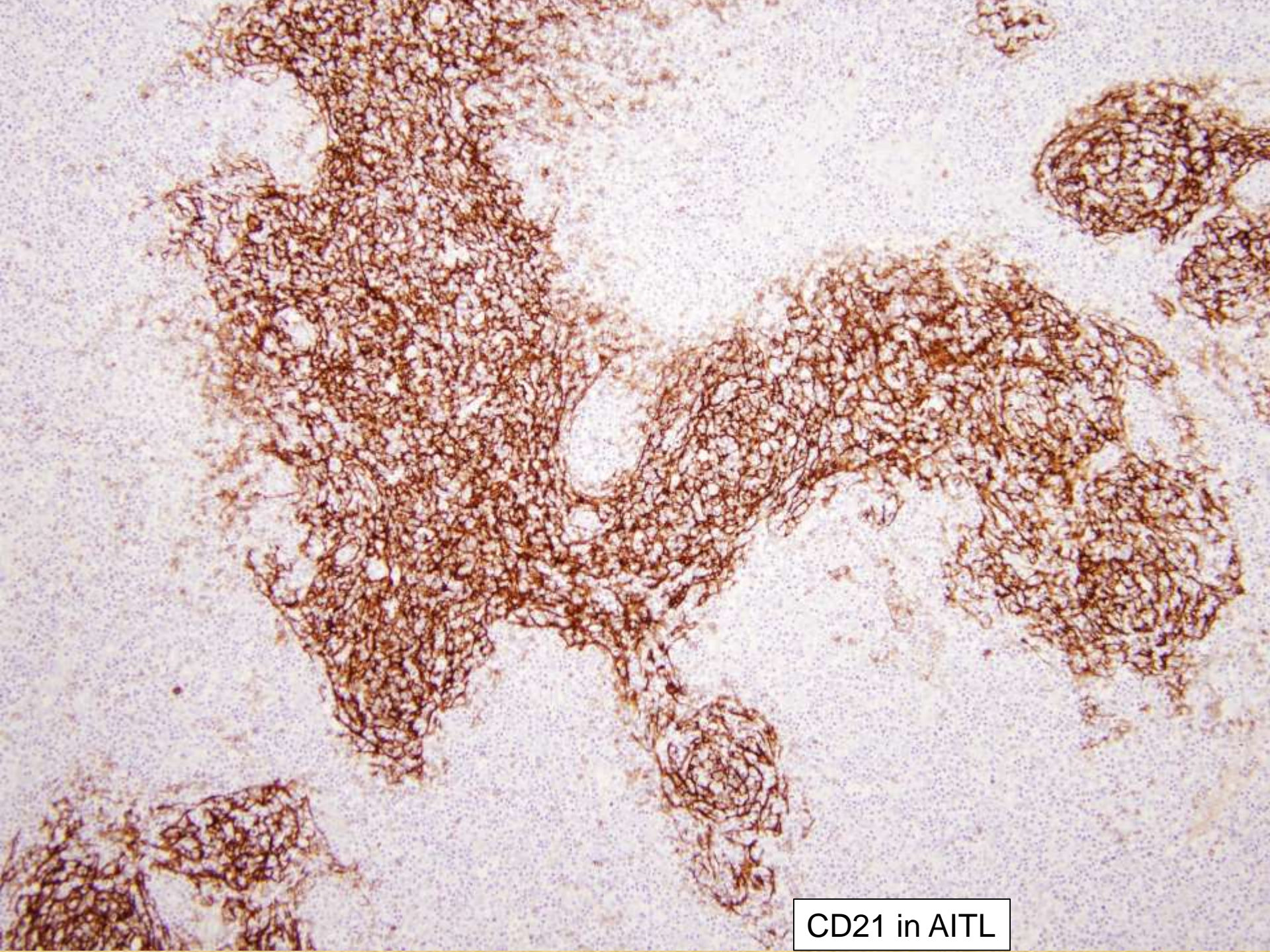
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**T follicular helper cell markers in lymphomas  
CD21 highlights expanded FDC networks in AITL**

### **Types of T follicular helper lymphomas:**

- Angioimmunoblastic T cell lymphoma
- Follicular T cell lymphoma
- Nodal PTCL with Tfh phenotype



CD21 in AITL



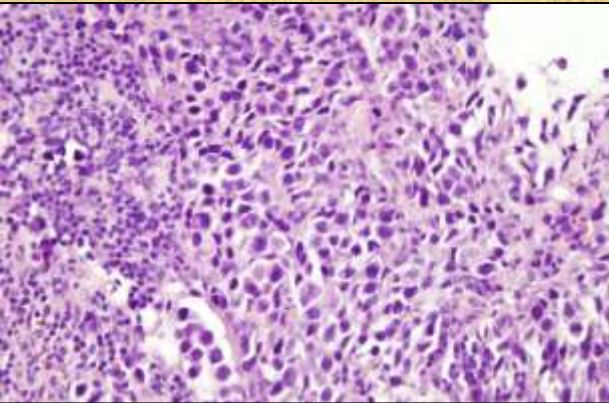
***Questions?***



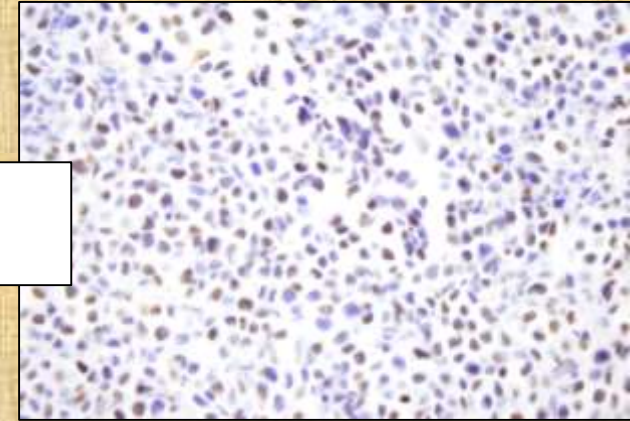
**[dennis.omalley@neogenomics.com](mailto:dennis.omalley@neogenomics.com)**



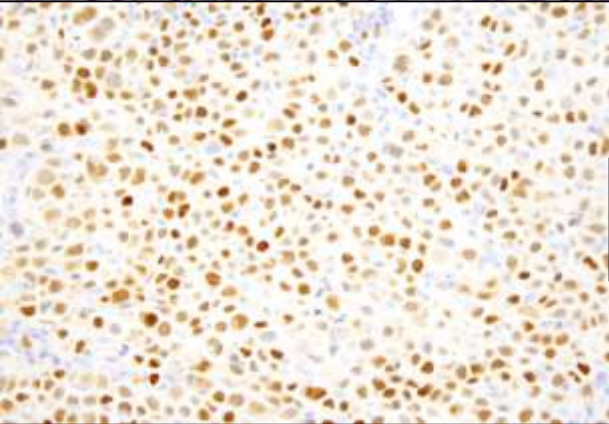
# IHC for Non-heme in Lymph Nodes



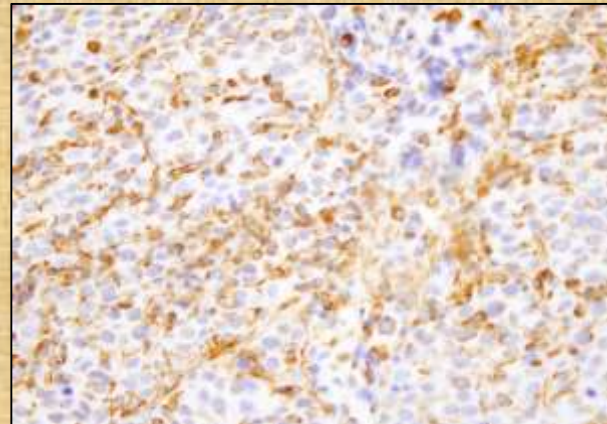
H&E



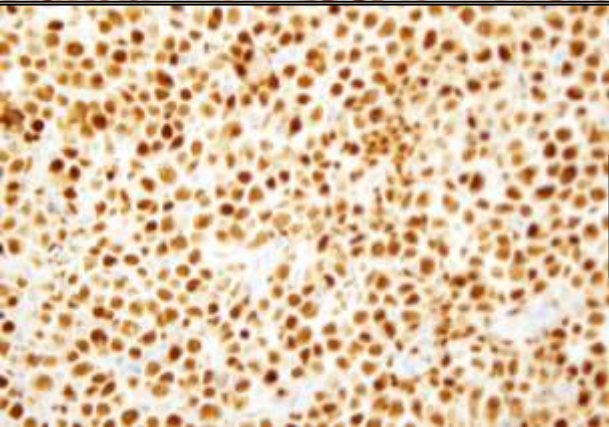
p53



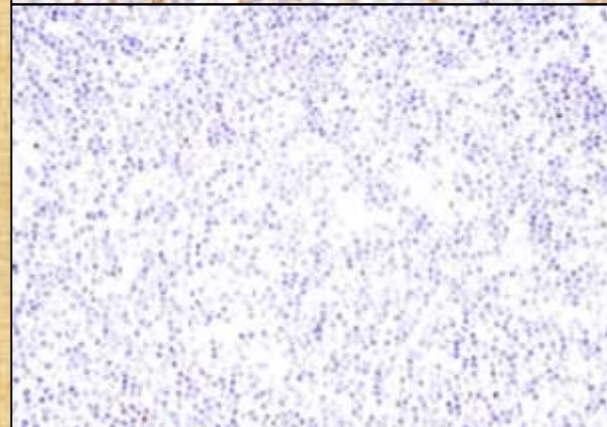
p63



Vim

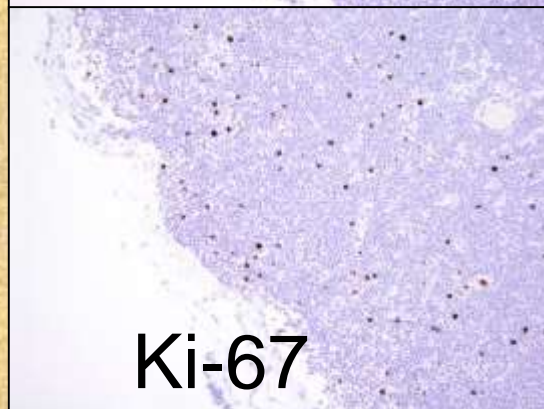
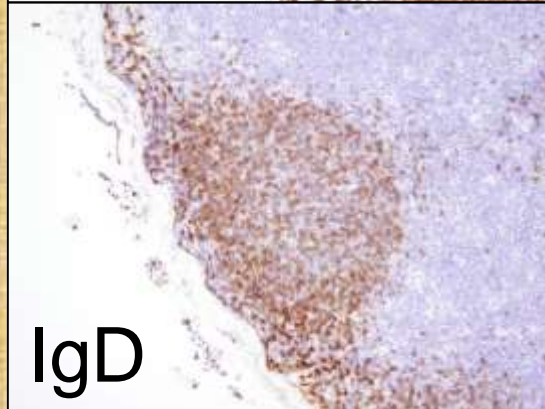
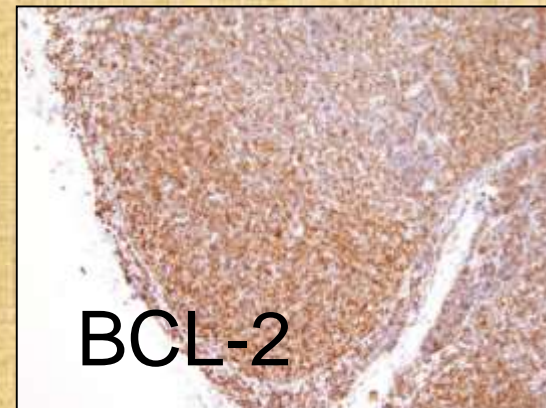
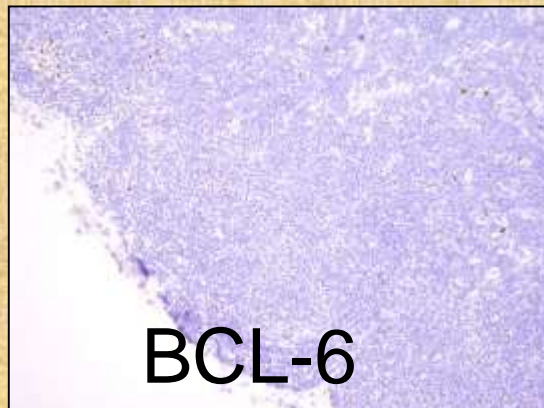
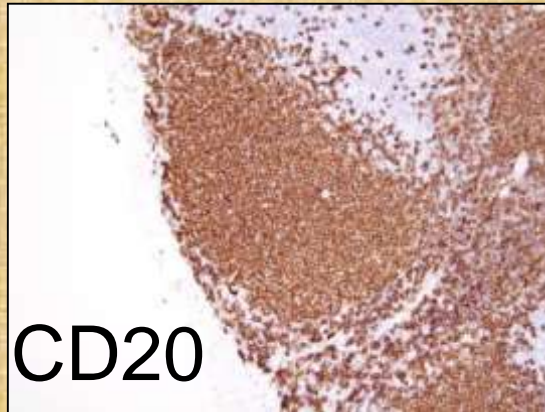


PAX8



GATA3

# Primary Follicles



Negative for Cyclin D1: These are *mantle cells* BUT NOT mantle cell lymphoma

[dennis.omalley@neogenomics.com](mailto:dennis.omalley@neogenomics.com)