ISIMM Tata Conference on Immunohistochemistry.

Kolkata, India, January 2018

Immunohistochemistry

A cost effective approach to lymphoma diagnosis

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University of Southern California

Disclosures; CRT –has consulting arrangements with for Philips, Agilent, PerkinElmer, Optra

IHC in LYMPHOMA

Practical Applications

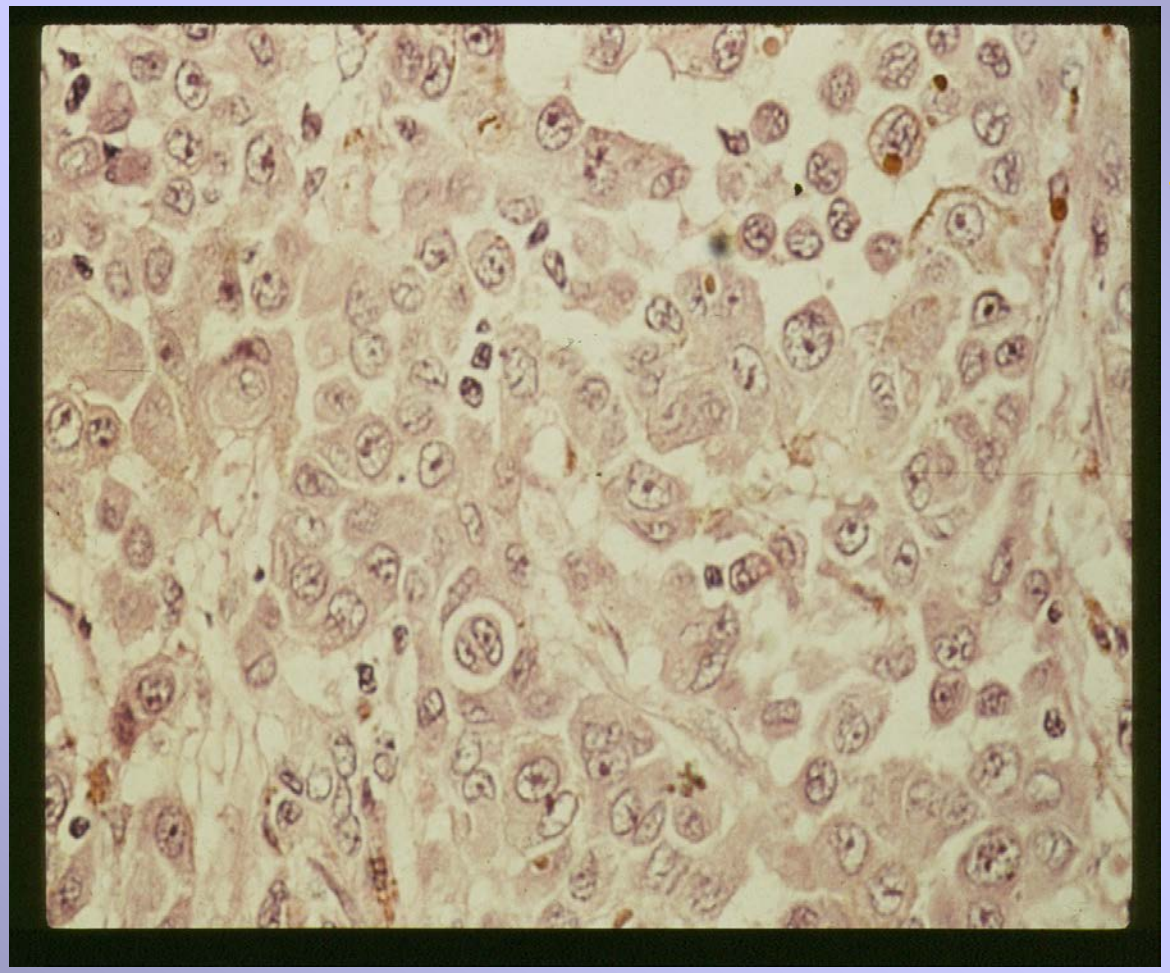
1. Lymphoma VS Anaplastic tumor

2. Reactive VS Malignant

3. Sub - classification, B VS T, HL VS Non-HL
   & specific types, CD1, ALK etc

4. Prognostic markers & predictive markers Inc PDL1

5. Micrometastases in nodes and marrow



ANAPLASTIC TUMOUR

discussed elsewhere

IHC stains

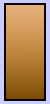
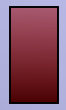
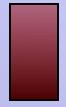
Carcinoma??

Lymphoma??

Melanoma??

Sarcoma??

ANAPLASTIC TUMOR

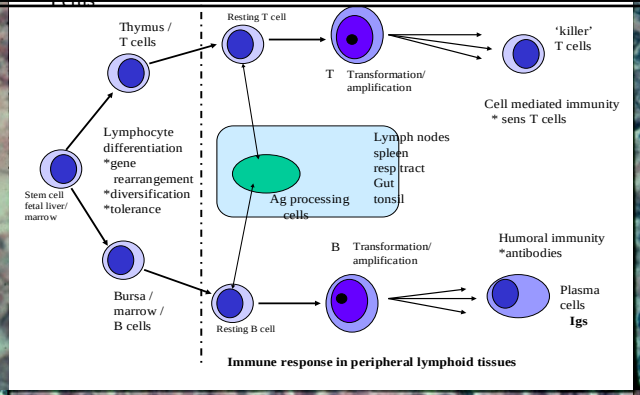
	carcinoma	sarcoma	lymphoma	melanoma
keratin				
vimentin				
CD 45				
S100				

Basic screening panel

CRT. USC.

Single cell lineage

Multiple morphologies



Author's personal copy

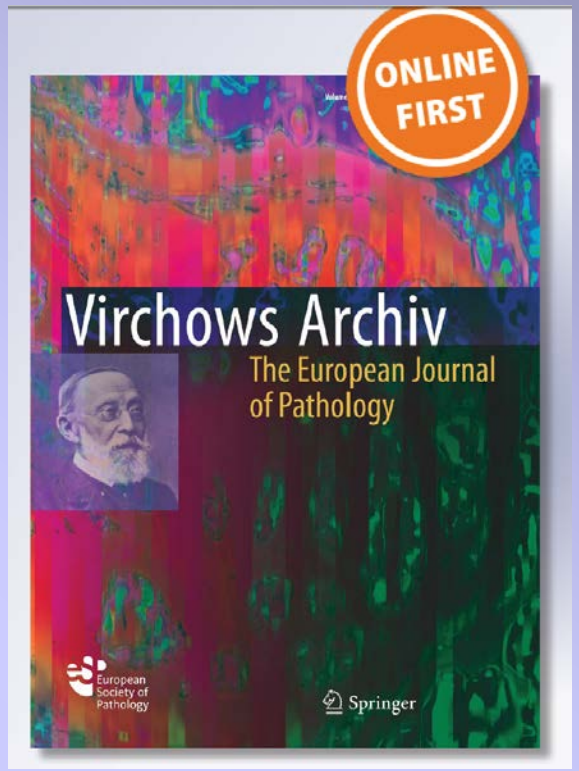
Virchows Arch
DOI 10.1007/s00428-013-1442-0

REVIEW AND PERSPECTIVES

Thomas Hodgkin: the "man" and "his disease": *humani nihil a se alienum putabit* (nothing human was foreign to him)

Stephen A. Geller · Clive R. Taylor

Virchows Arch (2013) 463:353–365



Beginning with Hodgkin in 1832 there have been numerous classifications of lymphoma.

Virchows Arch (2011) 458:637–648
DOI 10.1007/s00428-011-1083-0

REVIEW AND PERSPECTIVE

Classifications of lymphoma; reflections of time and technology

Clive R. Taylor · Robert J. Hartsock

THE FIRST “LYMPHOMA”

ON SOME

MORBID APPEARANCES

OF

THE ABSORBENT GLANDS

AND

SPLEEN.

BY DR. HODGKIN.

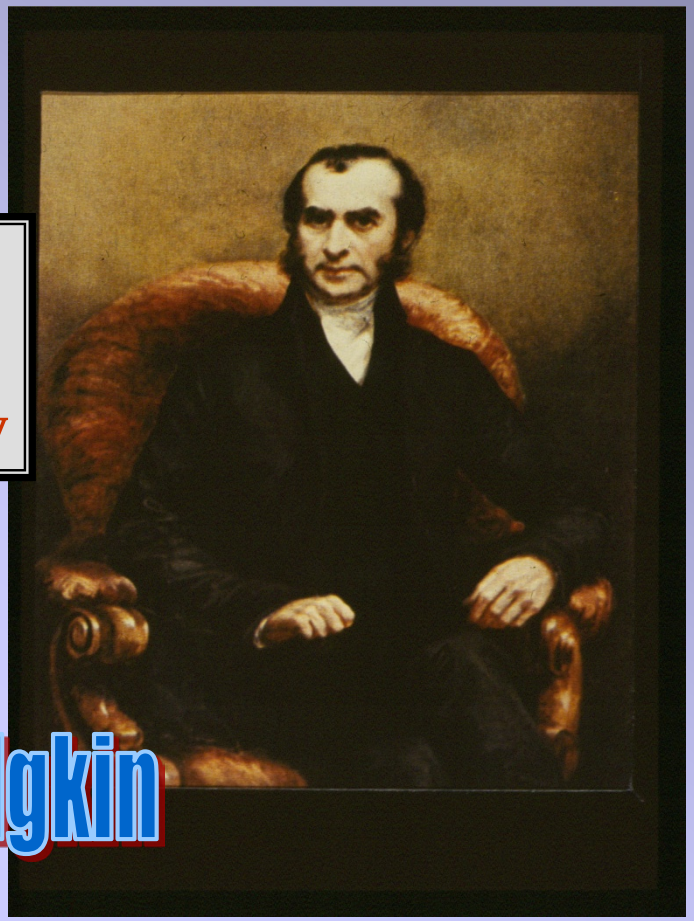
PRESENTED

BY DR. R. LEE.

READ JANUARY 10TH AND 24TH, 1832.

THE morbid alterations of structure which I am about to describe are probably familiar to many practical morbid anatomists, since they can scarcely have failed to have fallen under their observation in the course of cadaveric inspection. They have not, as far as I am aware, been made the subject of special attention, on which account I am induced to bring forward a few cases in which they have occurred to myself, trusting that I shall at least escape severe or general censure, even though a sentence or two should be produced from some existing work, couched in such concise but expressive language, as to render needless the longer details with which I shall trespass on the time of my hearers.

7 autopsy Cases
No microscopy



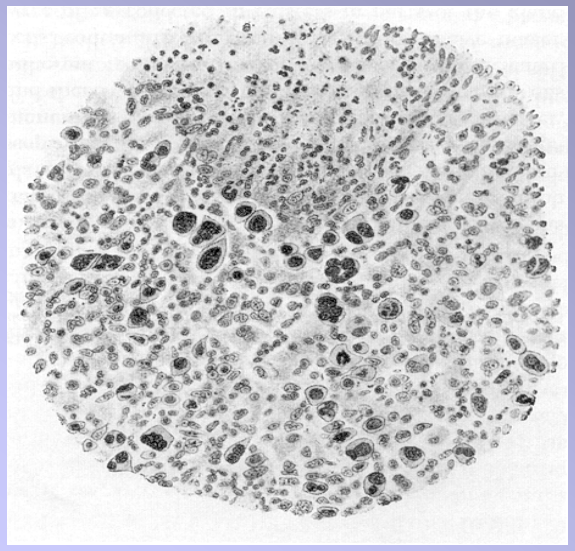
Thomas Hodgkin

1825- 1837

Inspector of the Dead
Curator of the Museum,
Guys Hospital, London.

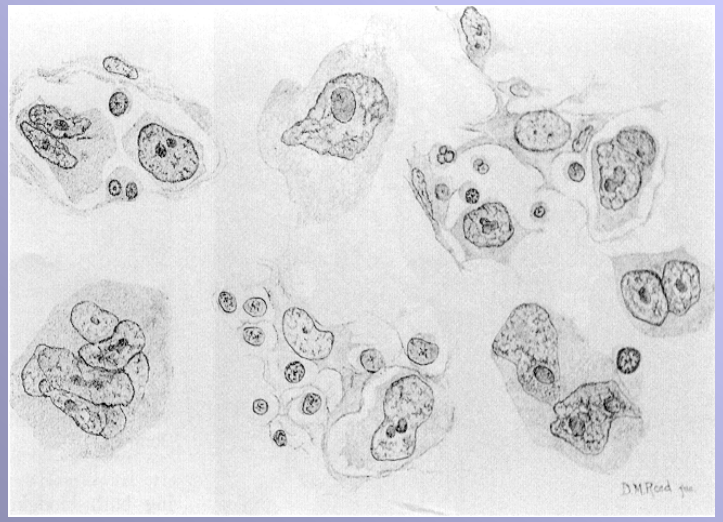
60 years later – the microscope makes its mark.

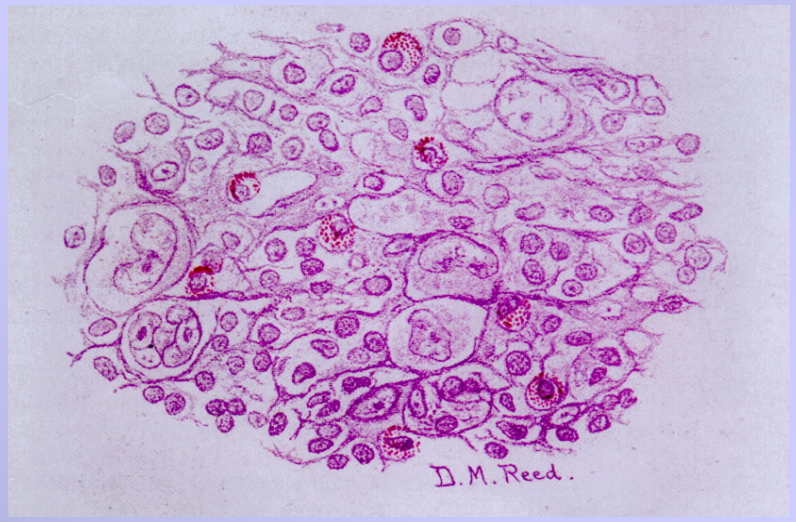
Sternberg Reed Cells



Sternberg, C. (1898)
Uber eine eigenartige unter dem Bilde der Pseudoleukamic verlaufende Tuberculose des lymphatischen Apparates.
Ztchr Heilk, **19,** 21-90

Reed, D. (1902)
On the pathological changes in Hodgkin's disease, with especial reference to its relation to tuberculosis.
Johns Hopkins Hospital Reports 10, 133-196





Lympho-sarkomatosis - 1903

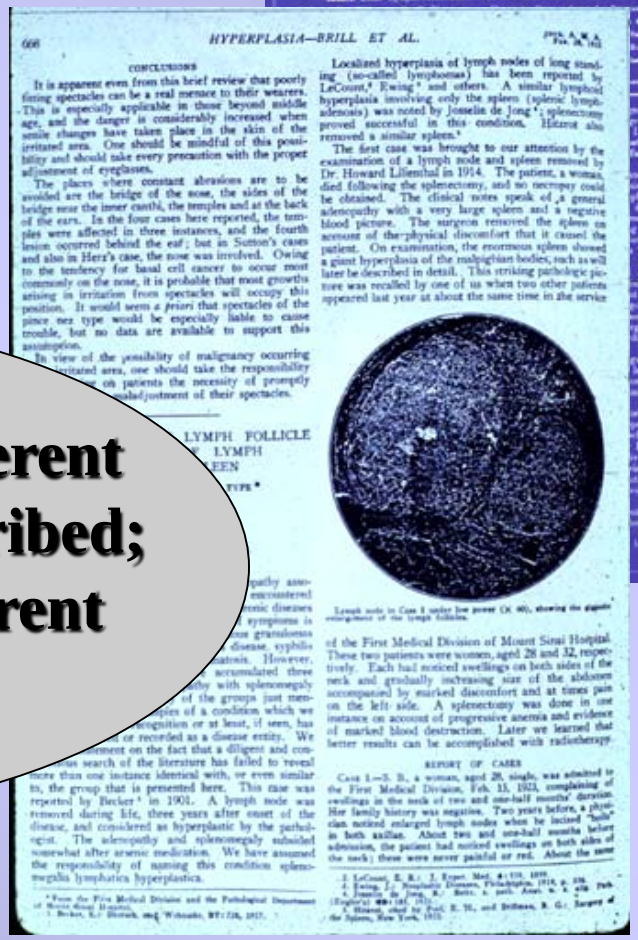
With advent of microscopy - many other ‘lymphomas’ were described – based upon morphology

By 1950 more than 50 different lymphomas had been described; and almost as many different classifications


Wiener klinische Wochenschrift

Organ der k. k. Gesellschaft der Aerzte in Wien.

VI. Jahrgang. Wien, 23. März 1893. Nr. 12.


HYPERPLASIA—BRILL ET AL.

CONCLUSIONS

Localized hyperplasia of lymph nodes of long standing (so-called lymphomas) has been reported by LeCount,[2] Ewing[3] and others. A similar lymphoid hyperplasia involving only the spleen (splenic lymphadenosis) was noted by Josselin de Jong[4]; splenectomy proved successful in this condition. Hitzrot also removed a similar spleen.[5]

The first case was brought to our attention by the examination of a lymph node and spleen removed by Dr. Howard Lilienthal in 1914. The patient, a woman, died following the splenectomy, and no necropsy could be obtained. The clinical notes speak of a general adenopathy with a very large spleen and a negative blood picture. The surgeon removed the spleen on account of the physical discomfort that it caused the patient. On examination, the enormous spleen showed a giant hyperplasia of the malpighian bodies, such as will later be described in detail. This striking pathologic picture was recalled by one of us when two other patients appeared last year at about the same time in the service

of the First Medical Division of Mount Sinai Hospital. These two patients were women, aged 28 and 32, respectively. Each had noticed swellings on both sides of the neck and gradually increasing size of the abdomen accompanied by marked discomfort and at times pain on the left side. A splenectomy was done in one instance on account of progressive anemia and evidence of marked blood destruction. Later we learned that better results can be accomplished with radiotherapy.

REPORT OF CASES

Case I.—S. B., a woman, aged 28, single, was admitted to the First Medical Division, Feb. 15, 1923, complaining of swellings in the neck of two and one-half months' duration. Her family history was negative. Two years before, a physician noticed enlarged lymph nodes when he incised a "boil" in both axillas. About two and one-half months before admission, the patient had noticed swellings on both sides of the neck; these were never painful or red. About the same

Giant Lymph Follicle Hyperplasia - 1927

For 100+ years Pattern Recognition

Metter et al. J Clin Oncol 3, 25, '85

Panel 7 pathologists - 'experts'.

Reviewed 105 follicular lymphomas

Diagnosis - small cell

consensus 39 cases, range 24 - 65 among the 7

Diagnosis - mixed cell

consensus 40 cases; all 7 unanimous in only ONE

In 37% of cases both small & large cell *were diagnosed by different members of the 7.*

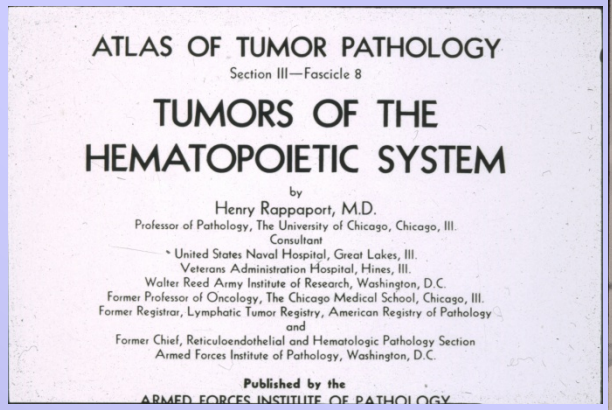
Diagnosis by Pattern Recognition

vol 29, 2061, 1996.

Accuracy versus consensus Dx.

Average panelist	**71 %**
Best panelist	**81 %**
Image Analysis*	**89 %**

**Using a continuous class approach, based upon SD cell/nuclear size, & measurements of high and low frequency diversity*


ATLAS OF TUMOR PATHOLOGY

Section III—Fascicle 8

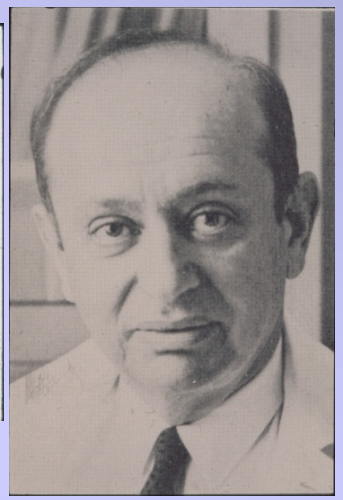
TUMORS OF THE HEMATOPOIETIC SYSTEM

by

Henry Rappaport, M.D.

Professor of Pathology, The University of Chicago, Chicago, Ill.
Consultant
United States Naval Hospital, Great Lakes, Ill.
Veterans Administration Hospital, Hines, Ill.
Walter Reed Army Institute of Research, Washington, D.C.
Former Professor of Oncology, The Chicago Medical School, Chicago, Ill.
Former Registrar, Lymphatic Tumor Registry, American Registry of Pathology
and
Former Chief, Reticuloendothelial and Hematologic Pathology Section
Armed Forces Institute of Pathology, Washington, D.C.

Published by the
ARMED FORCES INSTITUTE OF PATHOLOGY



Then from 1960-1990 we had the struggle to change classification basis from morphology alone --

Rappaport – histiocytic / lymphocytic

Bob Collins, Karl Lennert, Bob Lukes

To Immune based

The beginning of the WHO consensus process

To Immune based

Lymphoid neoplasms related to normal Lymphoid Development

IMMUNE BASED

TDT

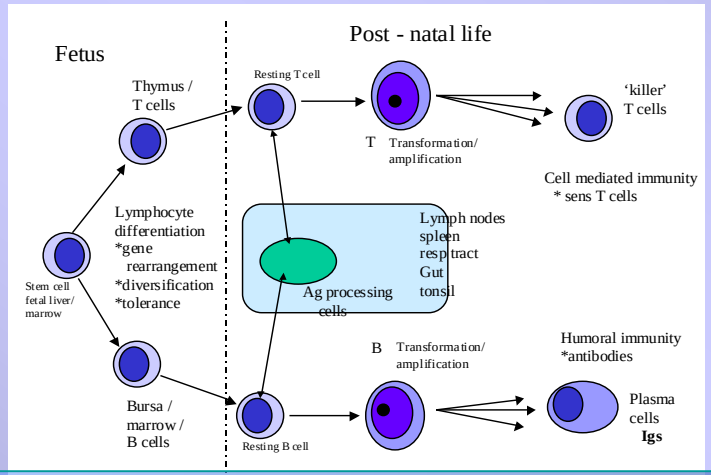
precursor

Stem cell TDT

precursor

TDT

CD2 CD3 CD4 CD5 CD8



Phenotype

Morphology

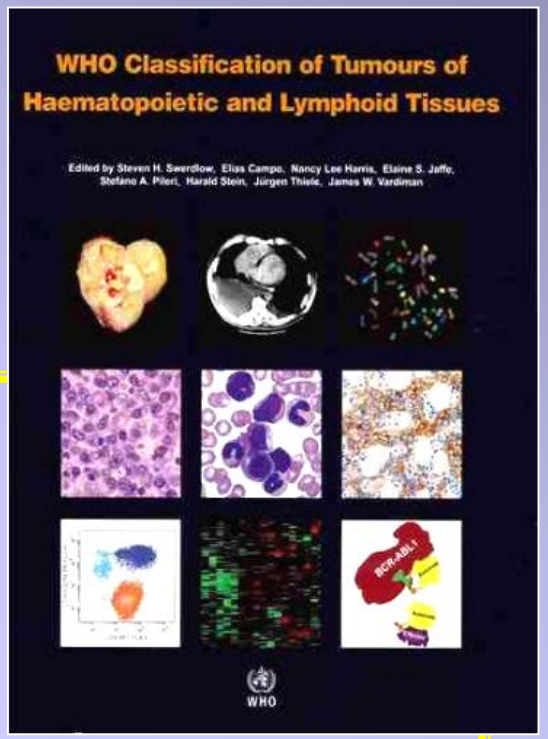
CD10 CD19 CD20 CD79

follicle

Who classification 2008.

6 main groups

72 + types



Precursor Lymphoid Neoplasms

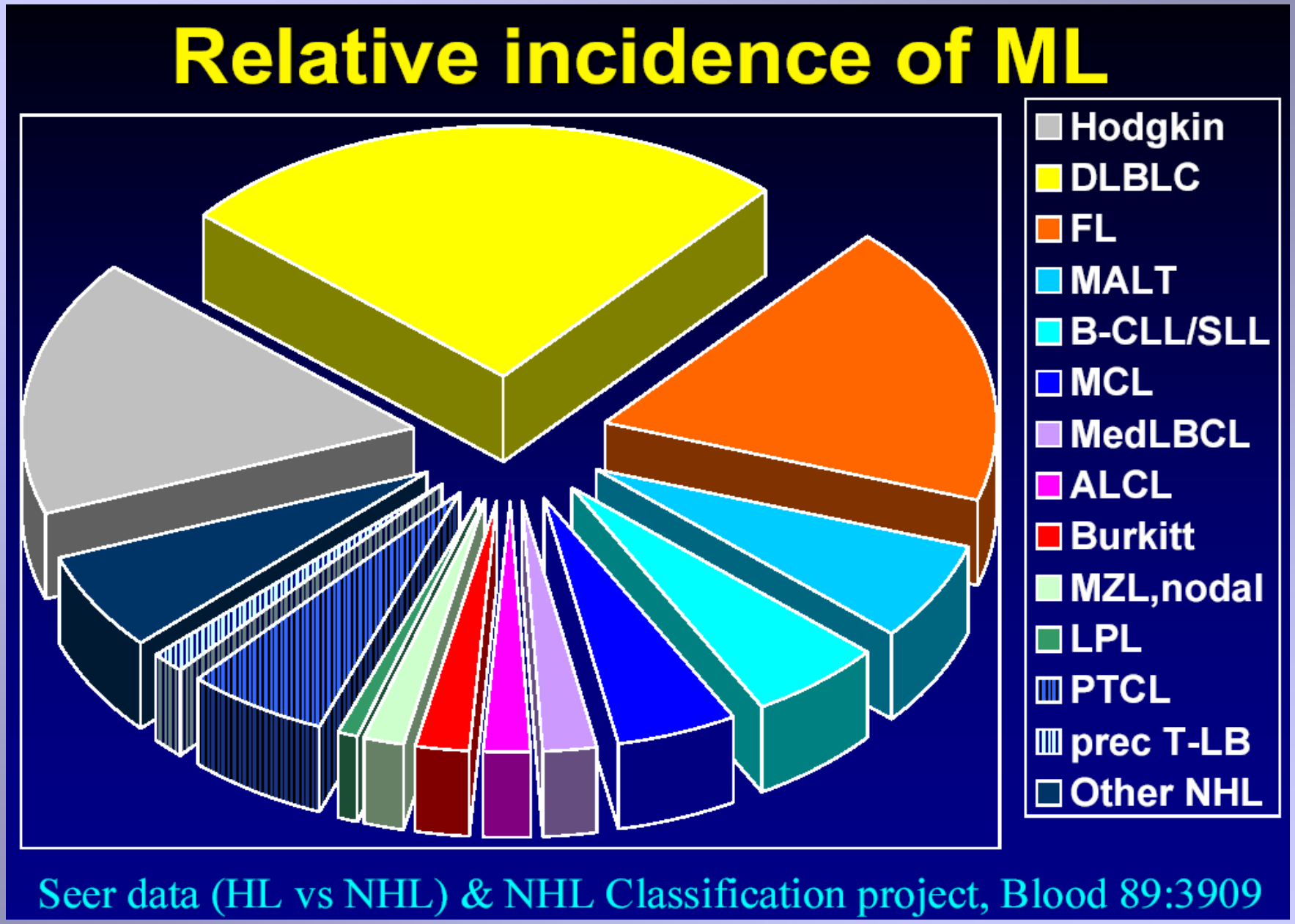
Mature B-Cell Neoplasms

Mature T-Cell & NK-Cell Neoplasms

Hodgkin lymphoma (Hodgkin disease)

Immunodeficiency-associated lymphoproliferative disorders

Histiocytic and Dendritic Cell Neoplasms



THE POINT-- 3 common types - rest uncommon (ADULTS).

Who classification 2008 – main types

C R Taylor 2009

	B types	T types
Precursor	**B lymphoblastic leukemia / lymphoma**	**T lymphoblastic leukemia / lymphoma**
Mature	**B-Cell**: CLL, Hairy cell, Lymphoplasma, Myeloma, MALTOMA, Follicular, Mantle, Diffuse, Burkitt	**T & NK Cell**: NK cell, Adult T cell, Enteropathy Ass, M Fungoides, Sezary Syn, Peripheral T, Anaplastic Large
Hodgkin	Nodular LP Classic: Nod sclerosis, Mixed cell	
Immdeficiency-assoc	√	√
Histiocytic and Dendritic		

C R Taylor 2009

the basis Who classification 2008

Morphology

Small v large cell

Hodgkin v NHL

Follicular v diffuse

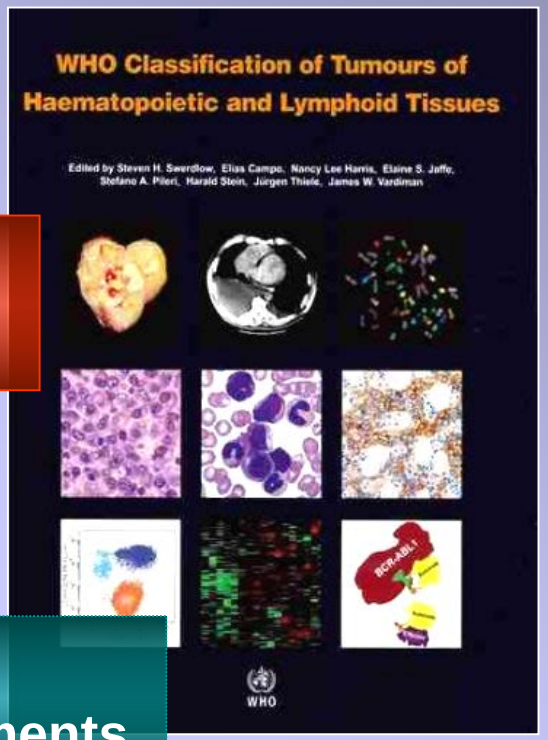
+ fine criteria

Phenotype

IHC B v T
80+ antibodies

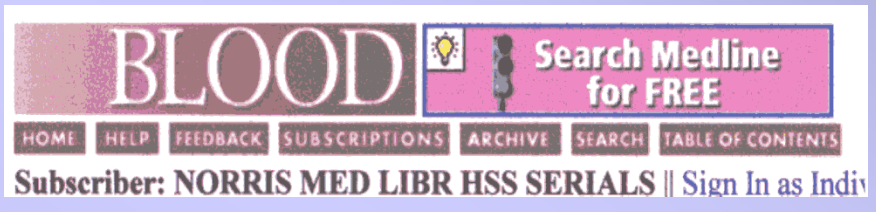
molecular

Translocations
Gene rearrangements



6 main groups

72 + types



89, 3909, 97

Expert agreement with consensus

	Histology only	+ IHC
Follicular - (by grade)	93 (60)	94 (61)
MALT / marginal z	84	86
small lymph / CLL	84	87
lymphoplasmacytoid	53	56
Burkitt (like)	47	53
mantle	77	87
diff Large B	73	87
precursor T	52	89
peripheral T	45	86
anaplastic large T/null	46	85

This assumes your IHC lab Is based on science NOT witchcraft -

Then lymphoma diagnosis is a more than just a magic trick ---

Assuming that most of these key leucocyte markers are validated in your lab

On paraffin sections

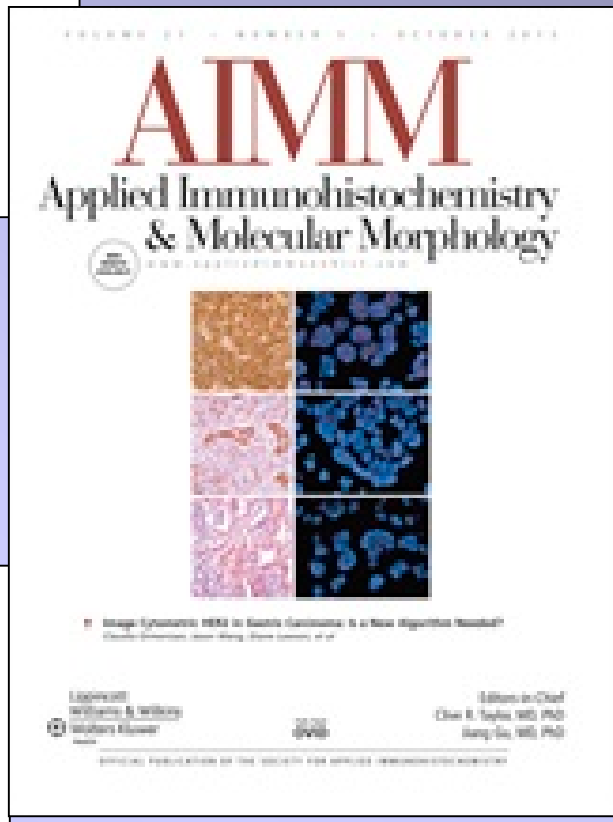
CD 45 - leucocyte common antigen

B	T	HL	H
CD20,CD79a, CD10,CD75, bcl 6, MUM1 CD138, myc cyclinD1, K,L CD19, PAX5 CD22,CD23 (bcl 2) (Annexin-A1 HCL) (cd5,cd43)	CD3 CD5,CD43 CD4,CD8, CD7 CD56 TIA-1 Gran B TdT [ALK]	(CD45) (EMA) CD30, CD15 BLA36, Fascin clusterin Pax5 CD40 LMP	CD68 CD163 CD11c lysozyme

IHC and the WHO Classification of Lymphomas Cost Effective Immunohistochemistry Using a Deductive Reasoning ‘‘Decision Tree’’ Approach

Clive R. Taylor, MD, DPhil

(Appl Immunohistochem Mol Morphol 2009;17:366–374)



The WHO Classification of Lymphomas: Cost-effective Immunohistochemistry Using a Deductive Reasoning‘‘Decision Tree’’ Approach Part II: Diffuse Patterns of Proliferation in Lymph Nodes

Clive R. Taylor, MA, MD, DPhil

(Appl Immunohistochem Mol Morphol 2009;17:470–482)

Diagnosis of lymphoma

4 decisions

4 methods

DECISIONS

***Reactive (‘benign’) vs malignant**

***Lymphoma (leukemia) vs metastasis**

***Hodgkin vs Non-Hodgkin**

***Sub-type, classification, B/T etc**

Morphology –gold standard

Phenotype – flow
IHC

Gene RX - Ig / TCR

Genotype – t(8;14), t(14;18)

Lymphoma

A dendrogram or 'decision tree'

Robb Smith, Taylor

"Lymph Node Biopsy" 1980

Morphology - - - abnormal architecture?

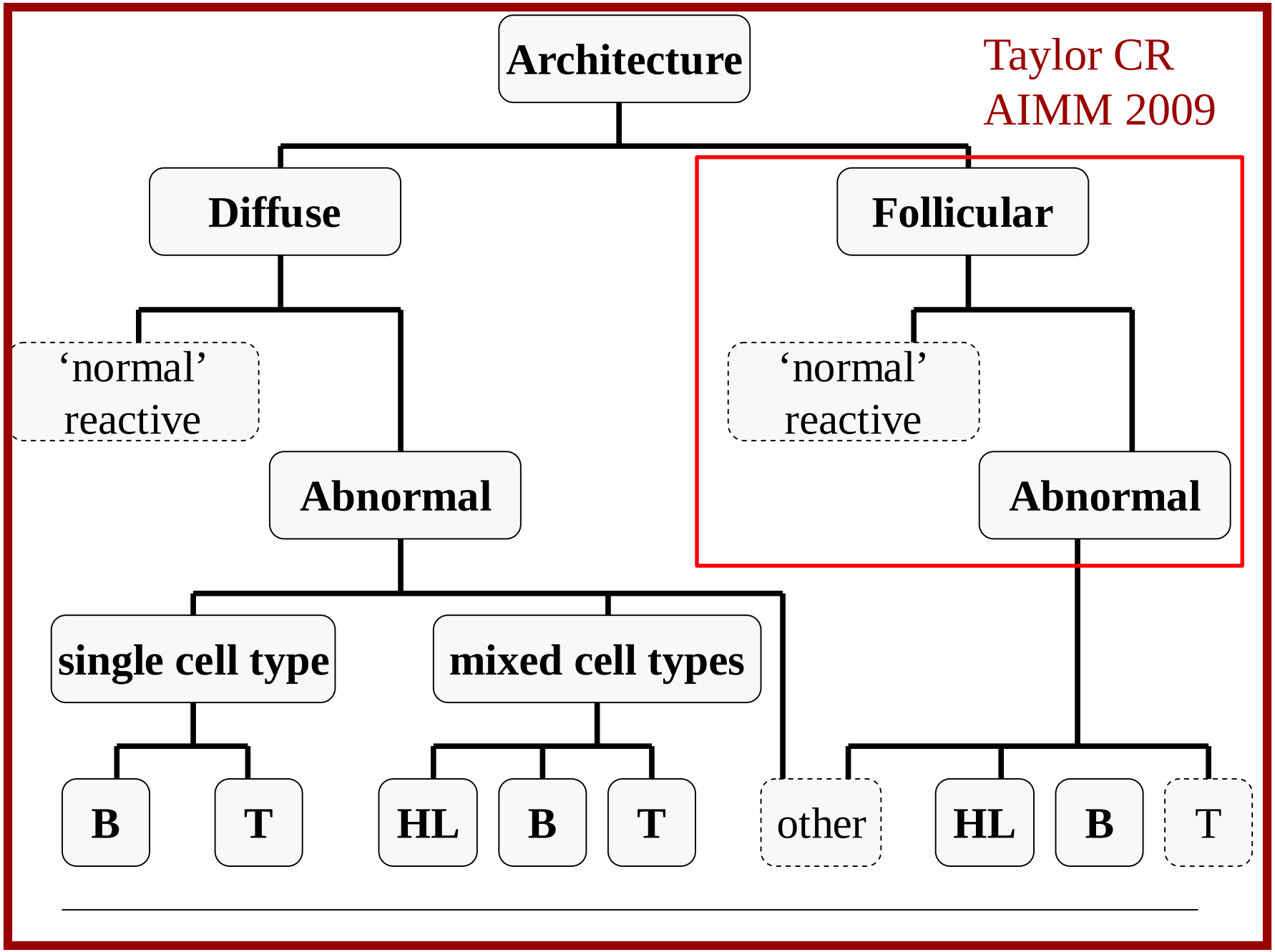
Diffuse or Follicular

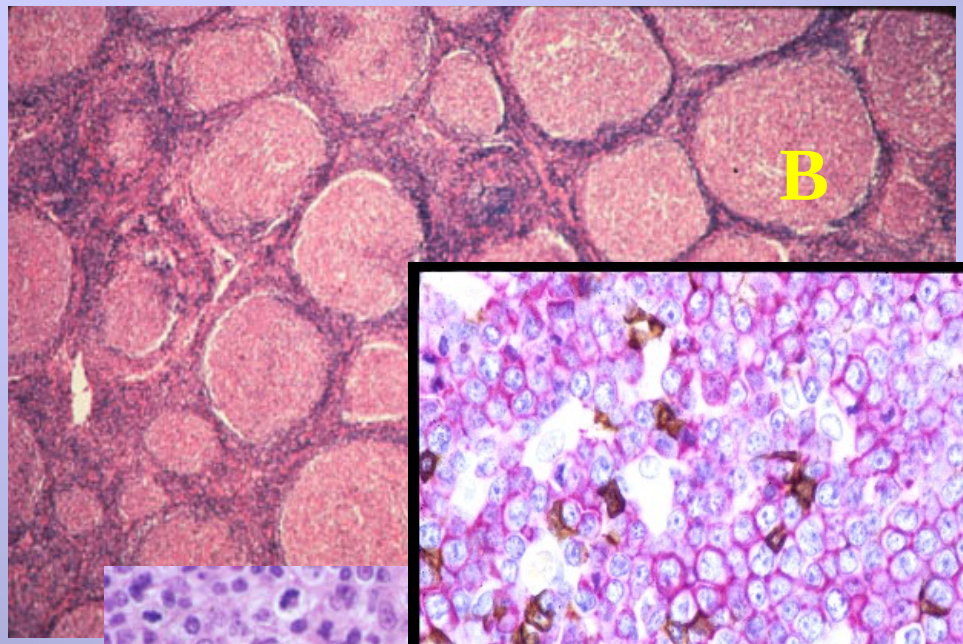
Single cell type

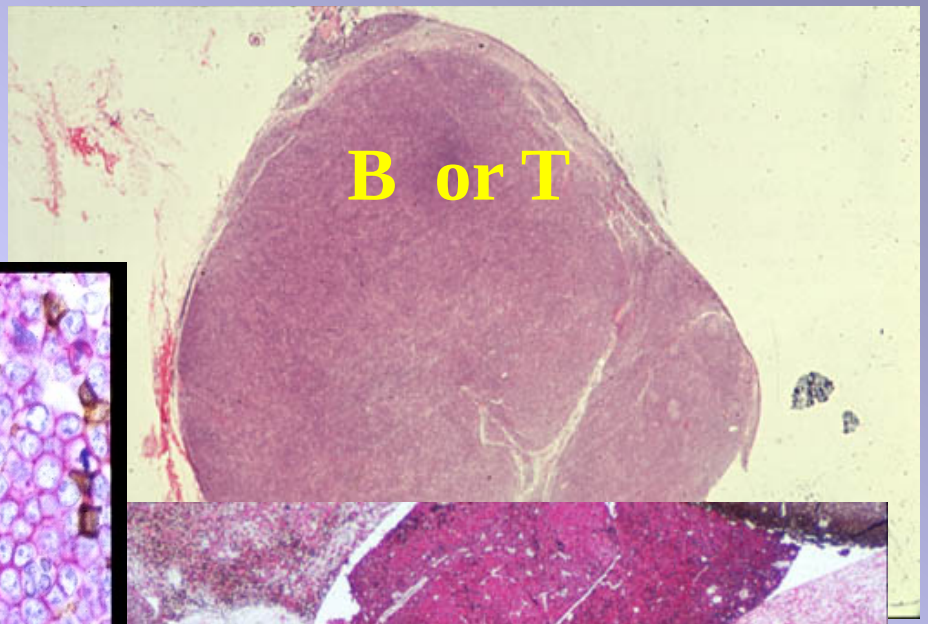
Mixture cell types

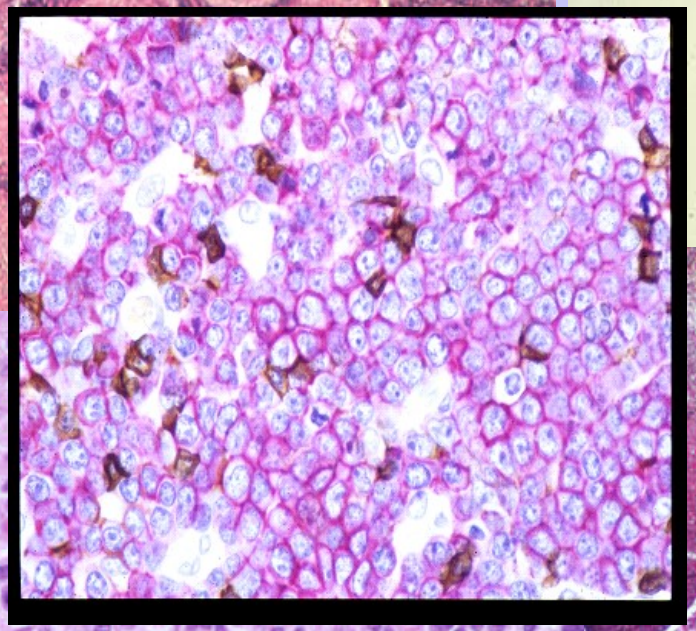
'gold' standard

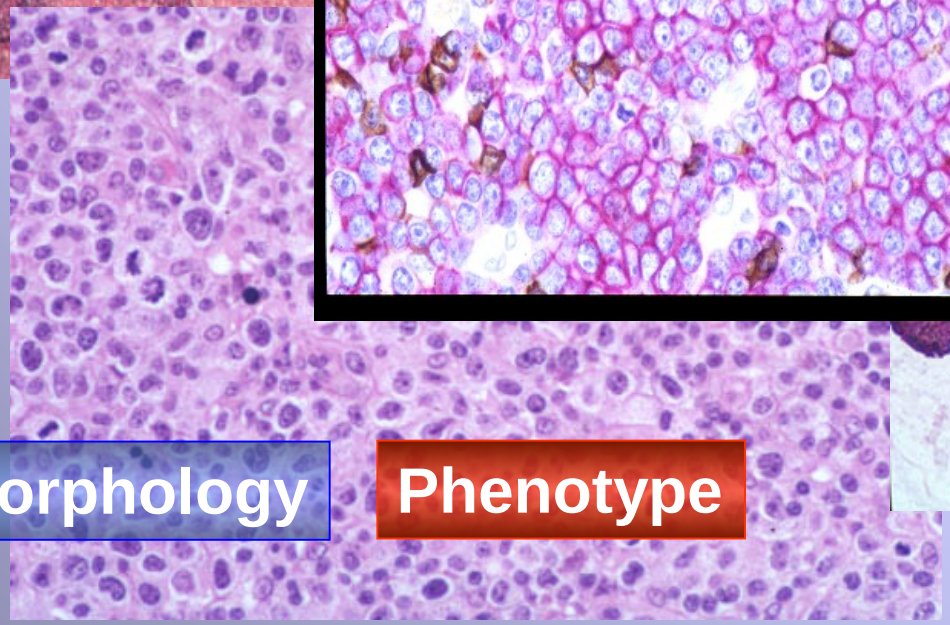
IHC molecular

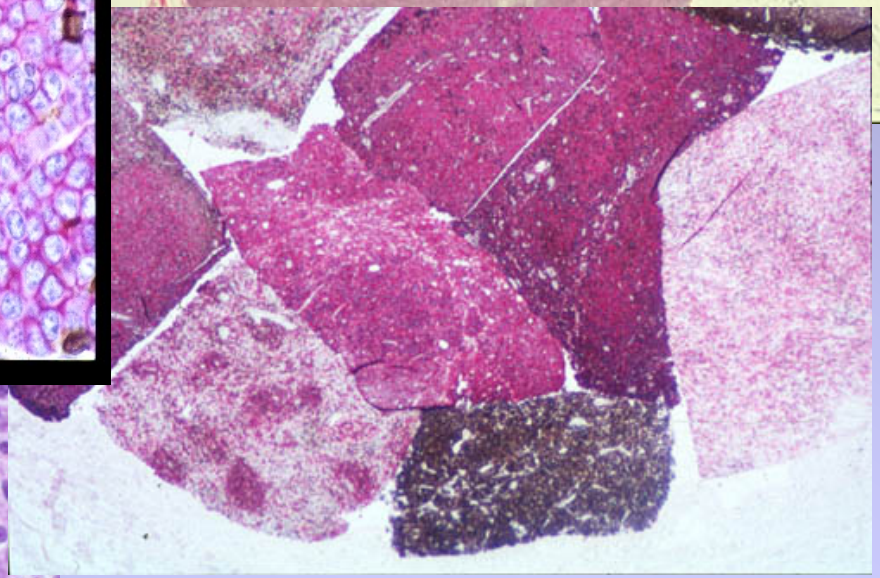

Architecture
Taylor CR
AIMM 2009
Diffuse
Follicular
‘normal’ reactive
‘normal’ reactive
Abnormal
Abnormal
single cell type
mixed cell types
B
T
HL
B
T
other
HL
B
T











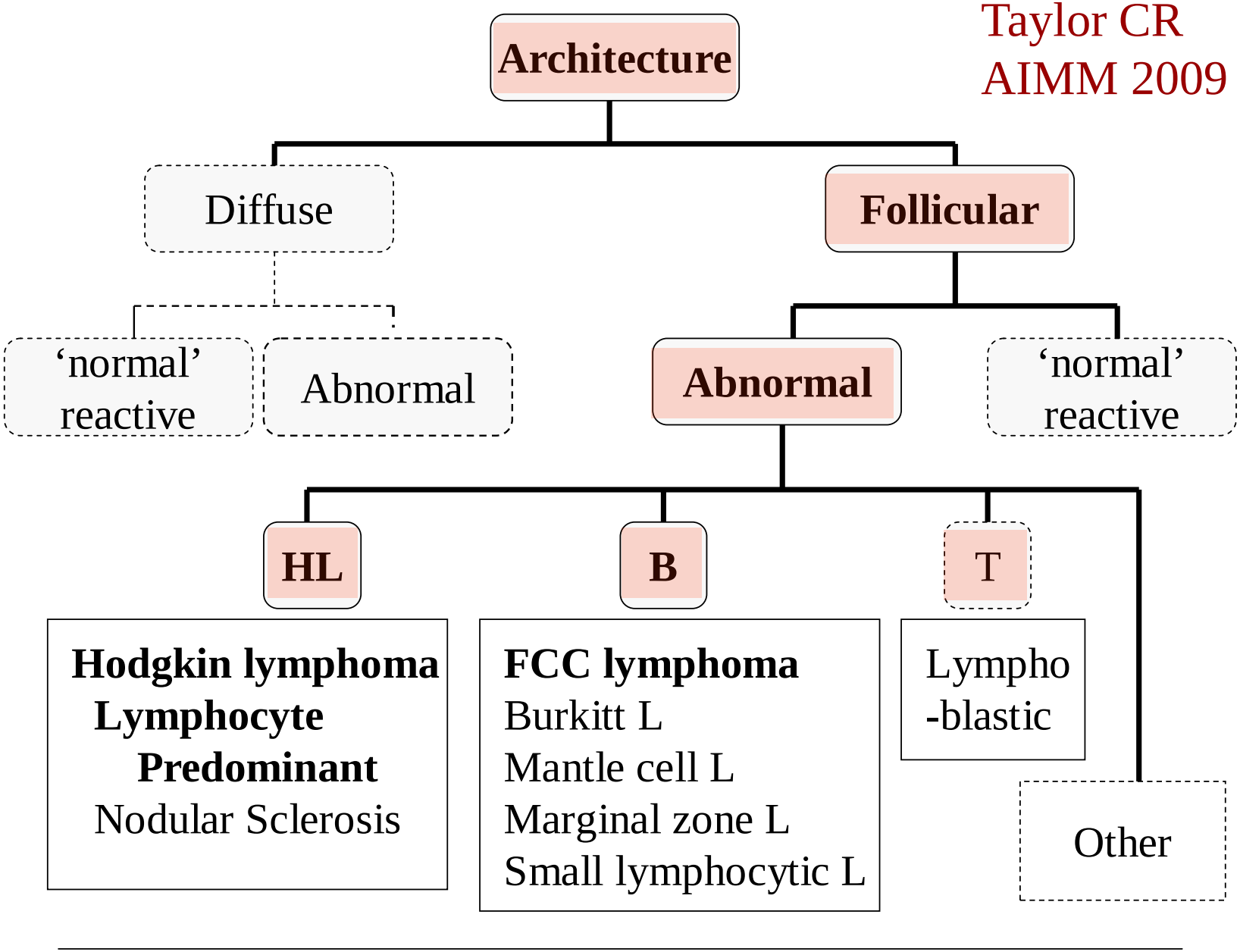
Morphology

Phenotype

B -red
T -brown

Immunohistochemistry (flow cytometry)

Taylor CR
AIMM 2009



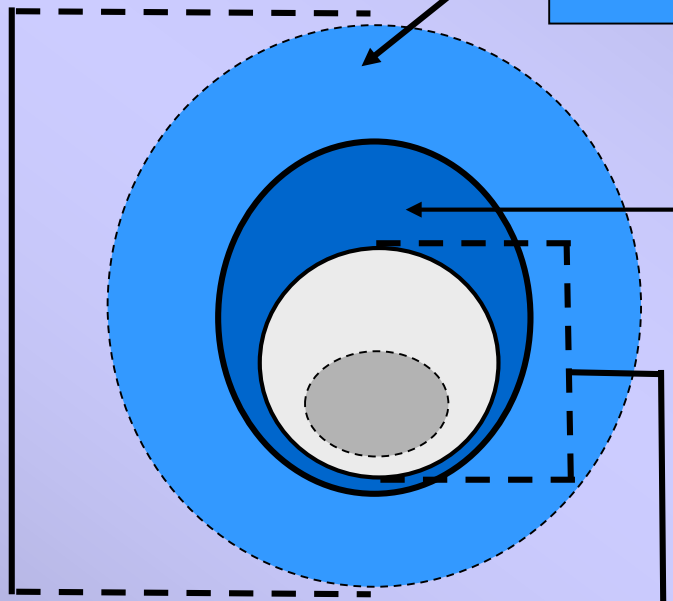
Reactive Follicle

Pan B +

Variable T cells
CD3+, CD5+ :
usually few
In mantle

Marginal Zone:
small lymphocytes
Pan B +
SIgM +

Mantle Zone:
small lymphocytes
Pan B +
SIgD+, SIgM+



Morphology

Phenotype

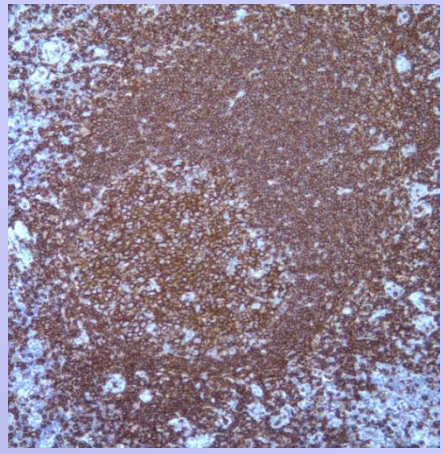
Reactive/germinal center:
larger cells
Pale zone – centrocytes
Dark Zone – centroblasts

Lymphocytes
Pan B+
CD10+
BCL6+
MUM1+/-
Ki67++

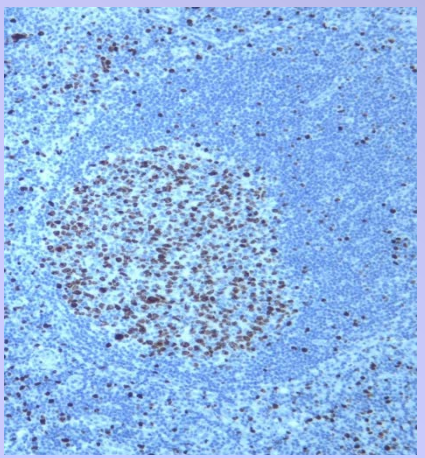
BCL2 neg

Dendritic cells
CD21+
CD35+

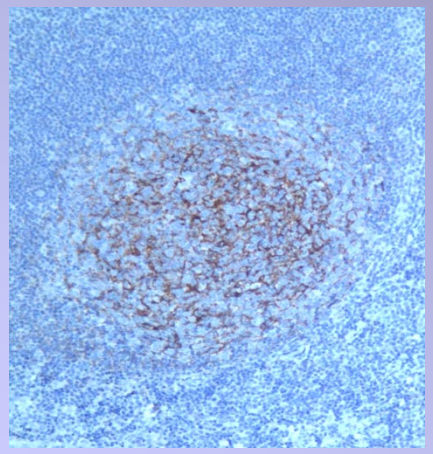
Histiocytes
CD68+
CD163+



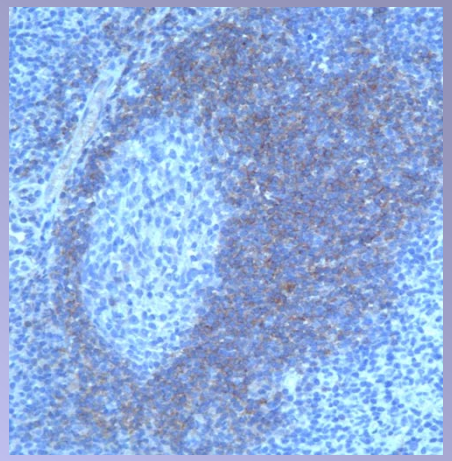
CD 20



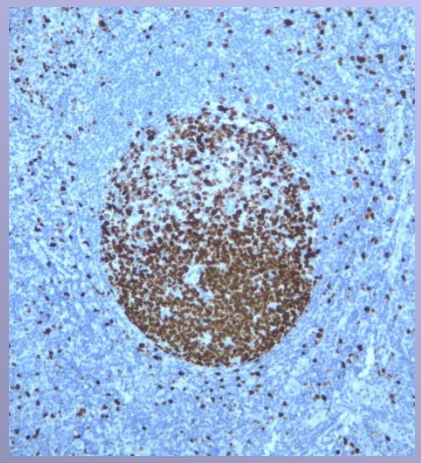
BCL6



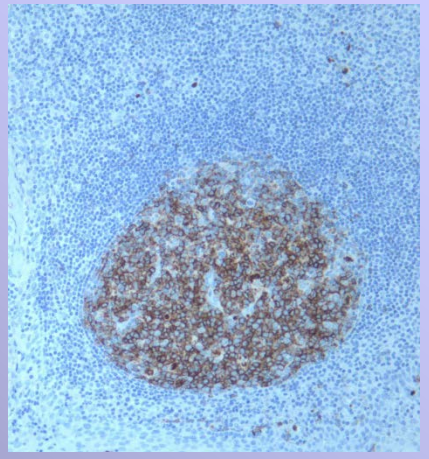
CD 21



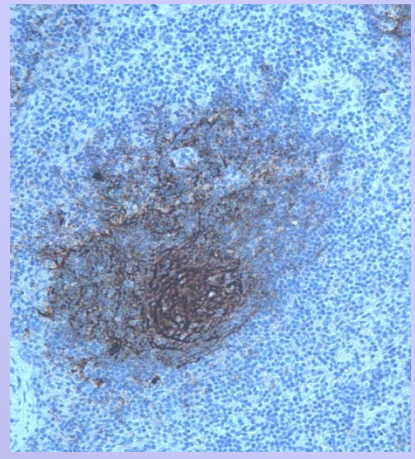
IgD



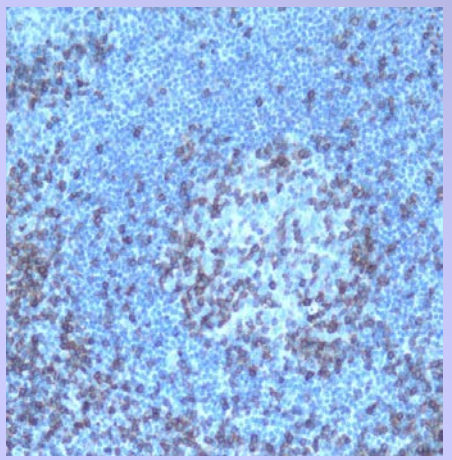
Ki67



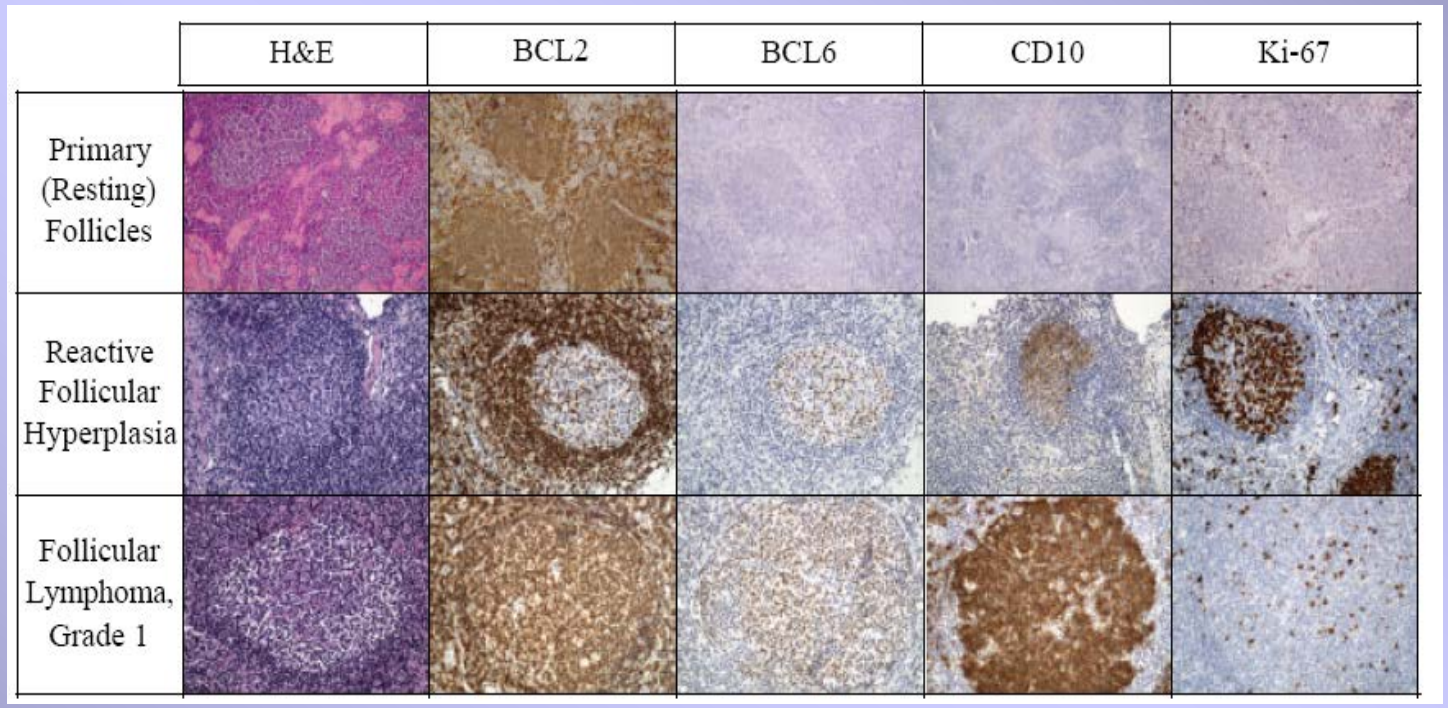
CD10



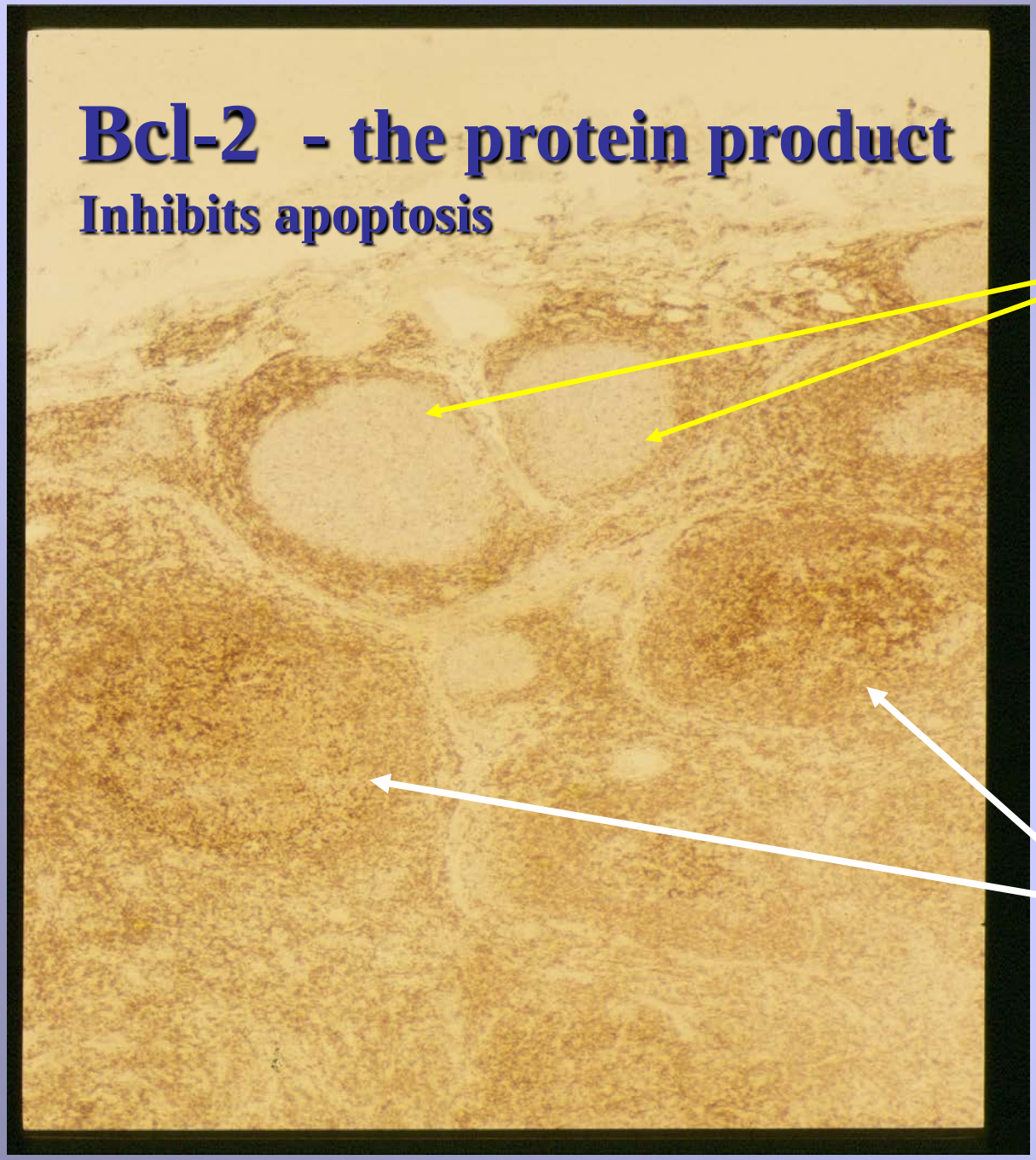
CD23



CD5



R. Miller 2003 – Propath.

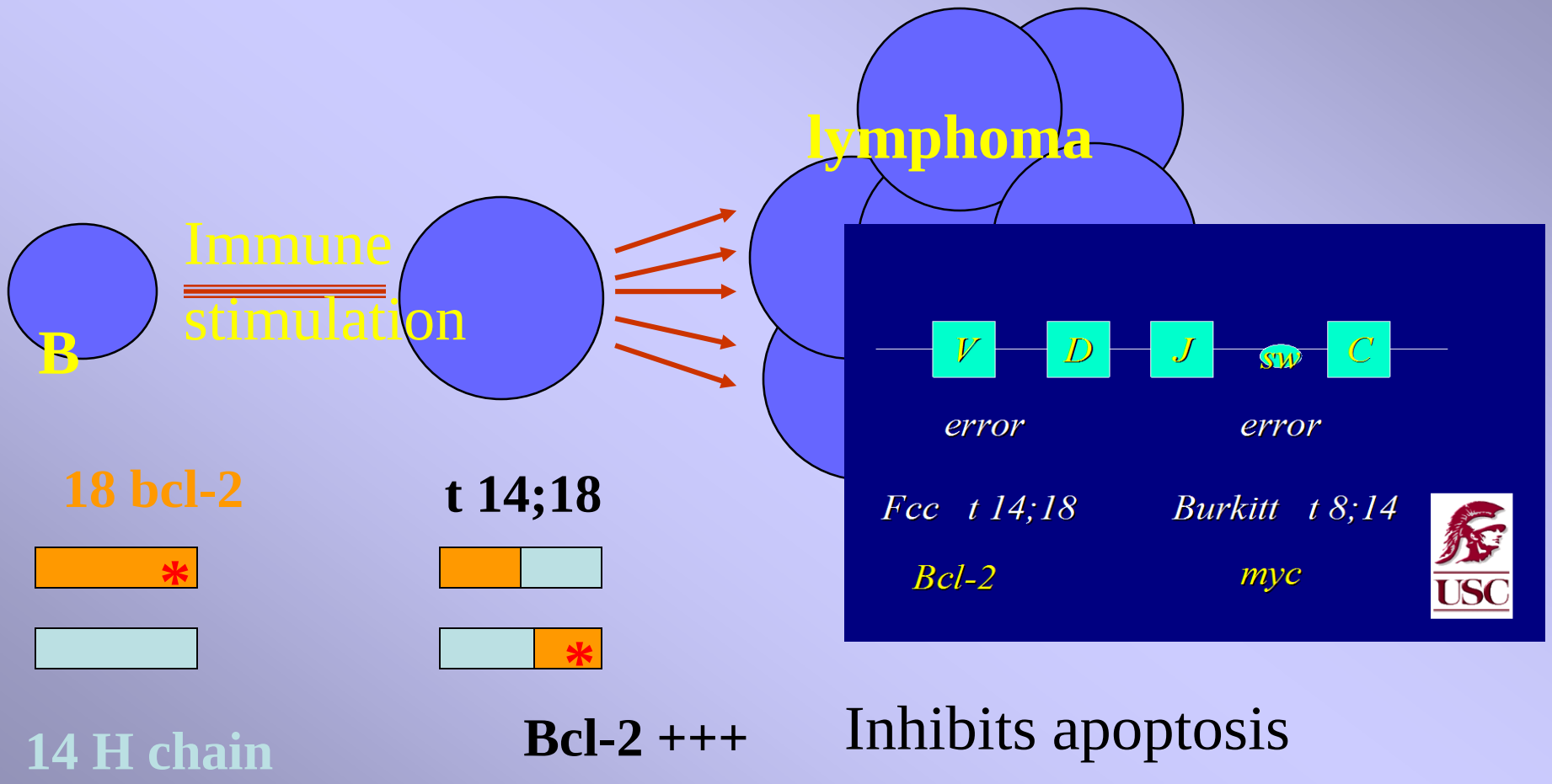


Reactive Follicles – negative

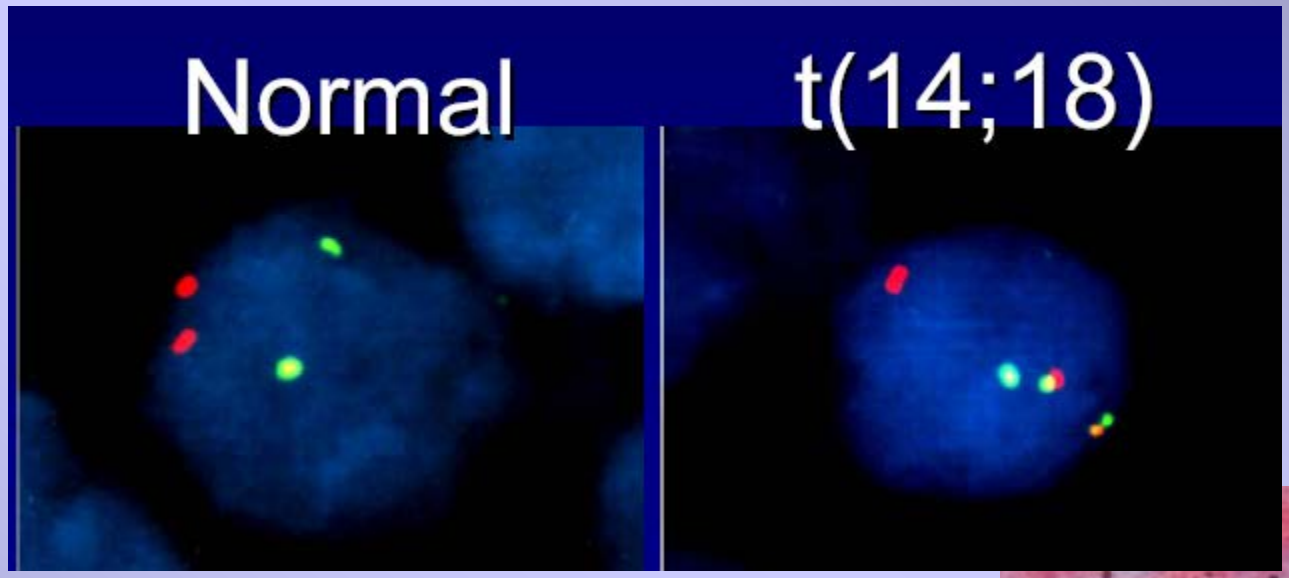
Neoplastic Follicles – positive

T(14;18)

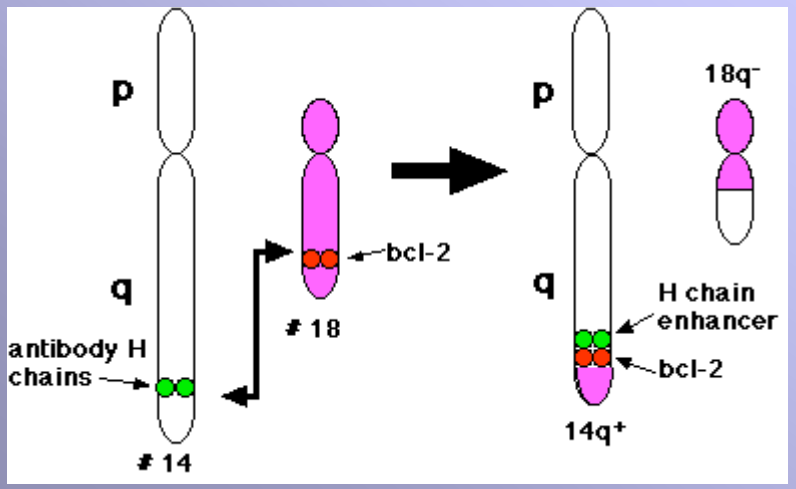
FCC lymphoma

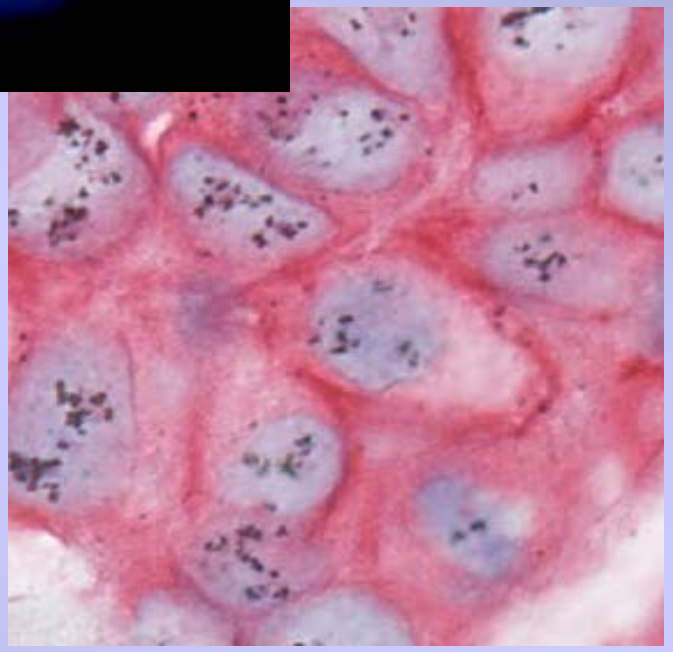


Inhibits apoptosis



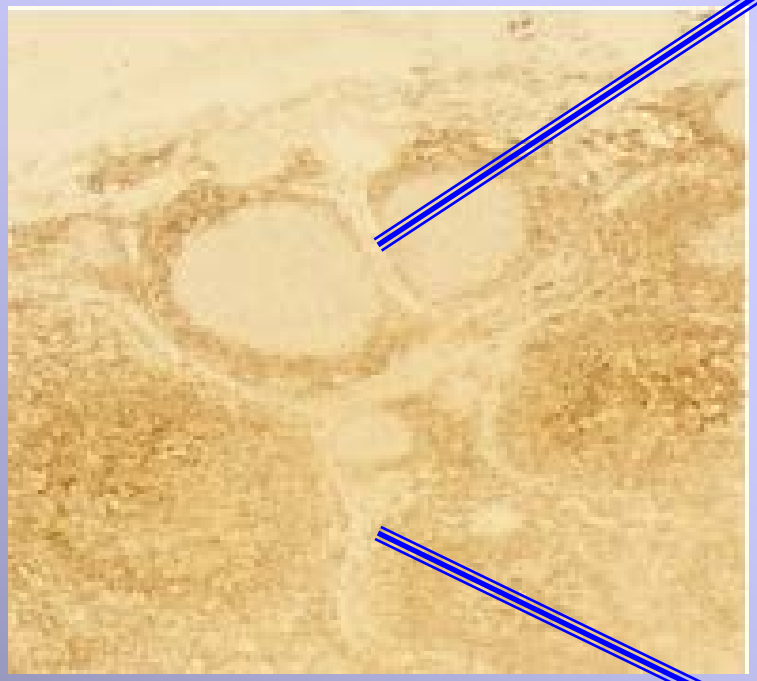
FISH Surti 2003



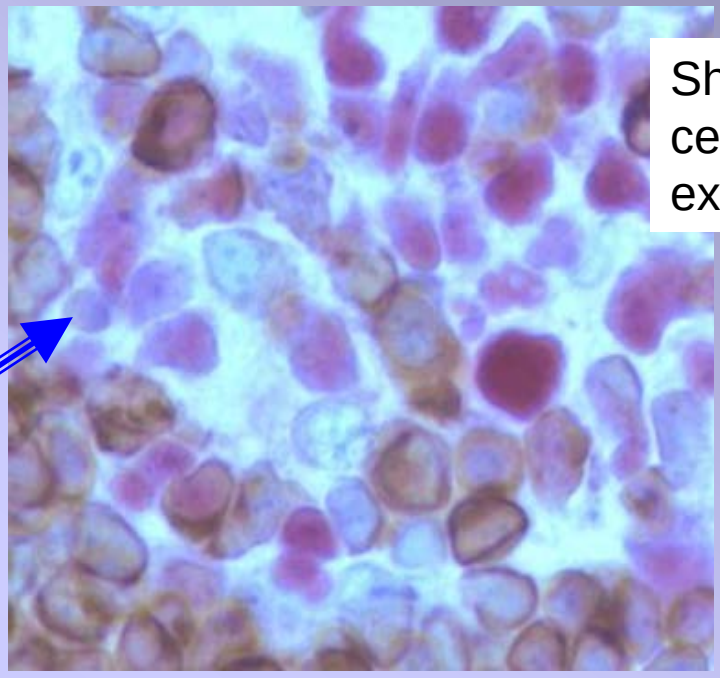


Goldfish -Tubbs 2001

Reactive Follicle ‘center’

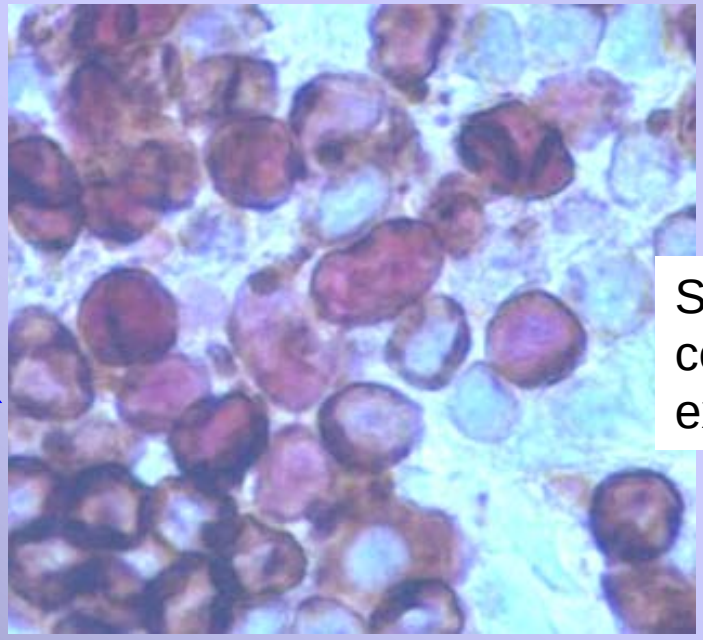


Neoplastic Follicle FCC lymphoma



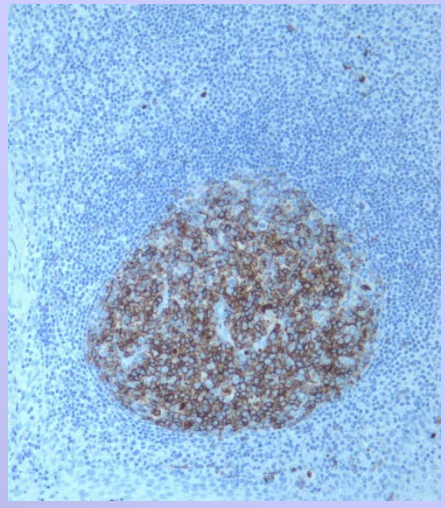
Shows ‘red’ FCC cells do not express BCL2

Bcl6 Red



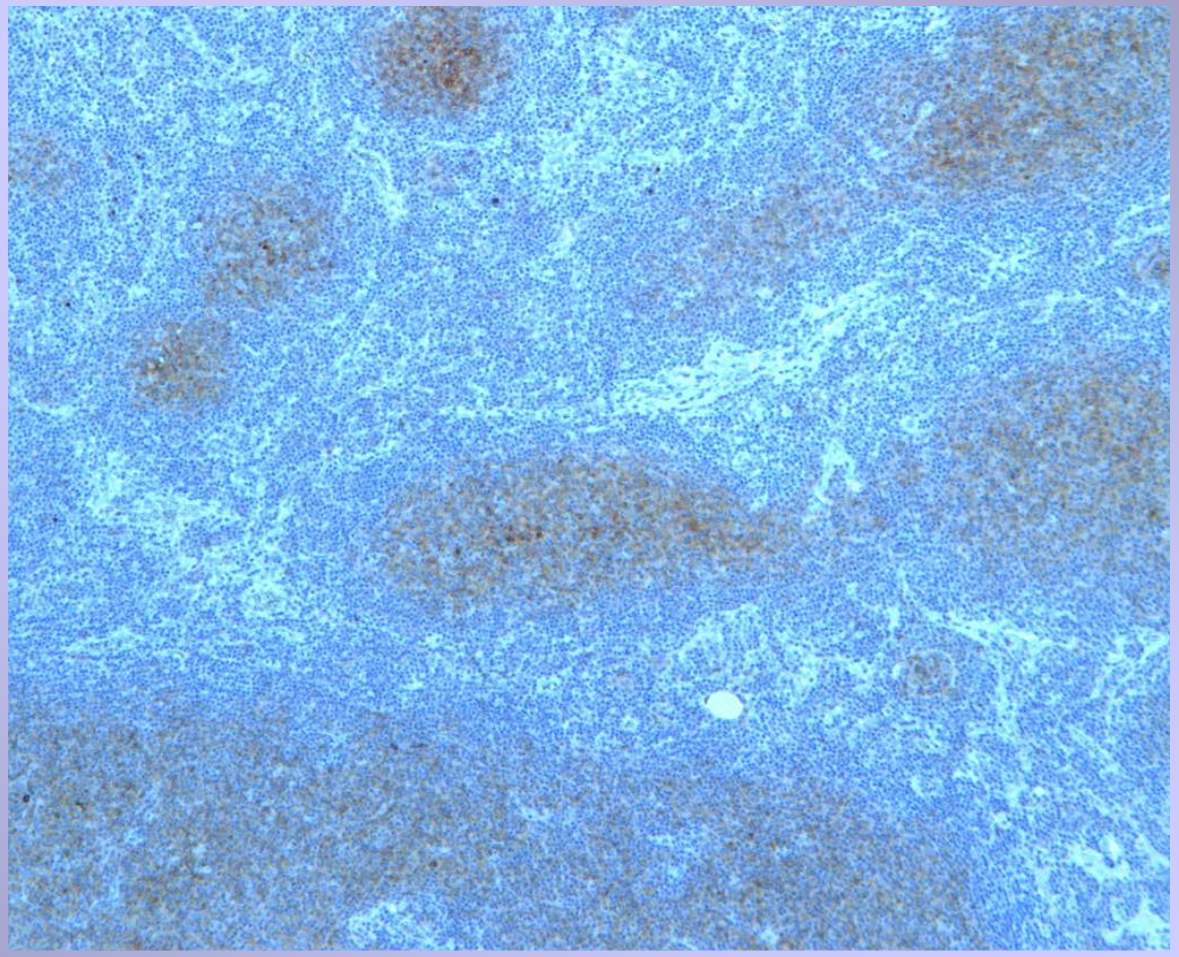
Bcl2 brown

Shows ‘red’ FCC cells express BCL2



CD10 REACTIVE

CD 10 FCC Lymphoma



CD10

Helpful with

loss polarity

and

extra-follicular
Diffuse areas

Summary - Follicular pattern

Differential

Reactive hyperplasia

B cell lymphoma

FCC

Burkitt

Mantle cell

Nodal Marginal

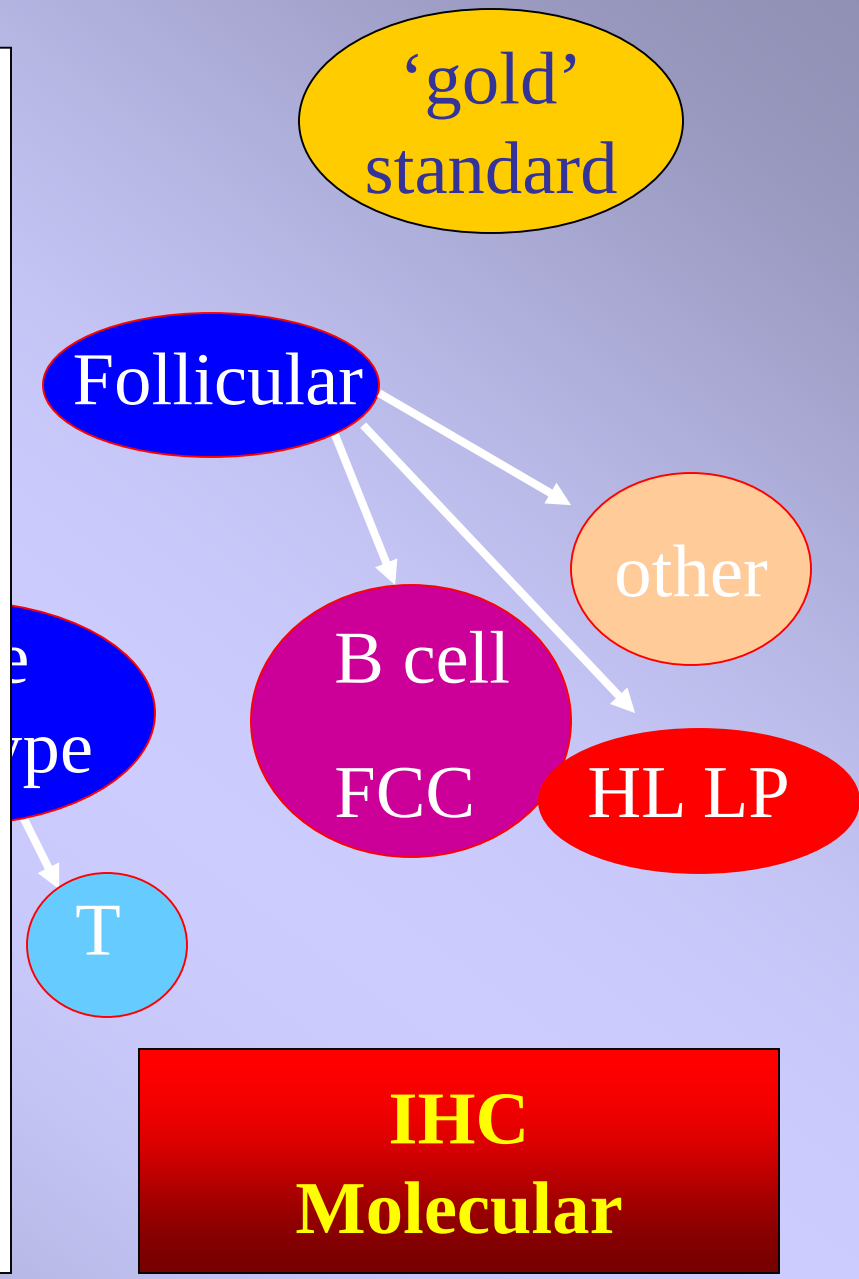
Small lymphocytic

Hodgkin lymphoma

LP

NS (classic)

T lymphoblastic lymphoma



Role of IHC

CD19,CD20
Pax5,CD79a
CD10, bcl 6,
(bcl 2)
cyclinD1,
K,L
CD23
(cd5,cd43)
PD-1

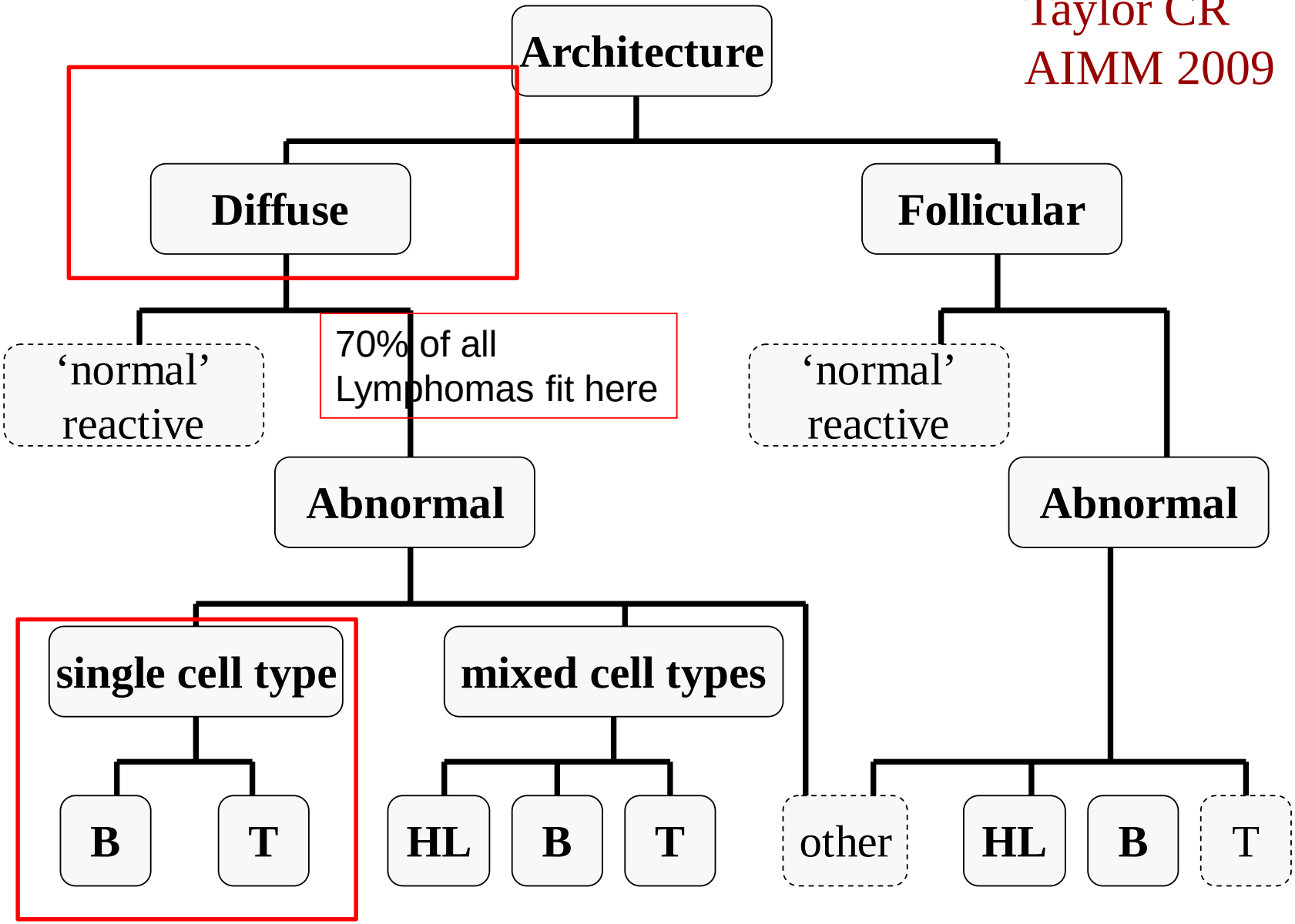
	Nod LP	FCC
CD45	+ RS	+
CD20	+	+
CD79a	+	+
bcl6	+	+
Pax5	+	+
EMA	+	-
bcl2	+/-	(+)
CD3	(++)	(+/-)
K/L clonal	(+)	(+)

+ mantle and marginal – under diffuse

Pay attention to the ‘follicles’

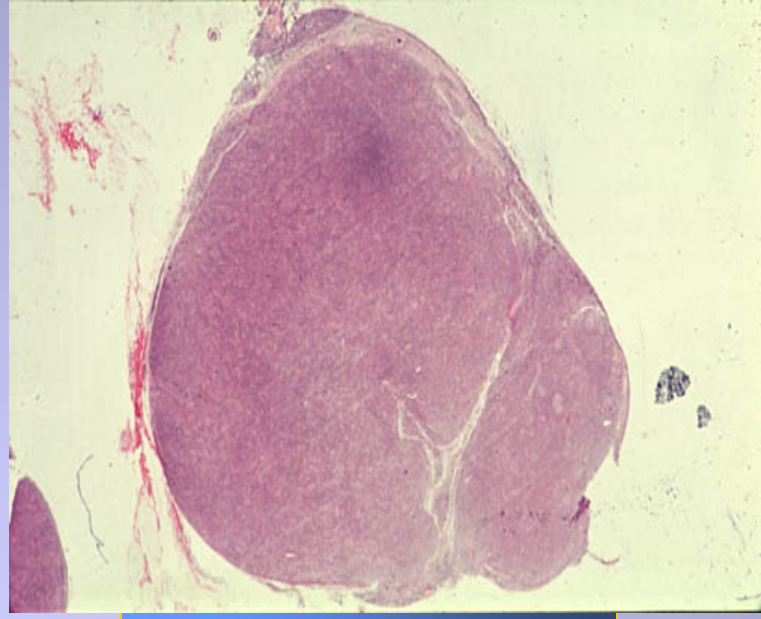
FOLLICULAR	Lymphoma markers		‘follicles’
Reactive hyperplasia	‘B’		**reactive***
B cell lymphoma			
FCC	**‘B’ CD10, BCL6 ------ BCL2+**		
Burkitt	‘B’ CD10, BCL6,-/+43 ----------		
Mantle cell	‘B’	Cyclin D1,CD5,43	reactive*
Marginal ‘Nodal’	‘B’	21, -/+43	reactive*
Small lymphocytic	‘B’	CD23, 5, 43	‘pseudo-’
Hodgkin lymphoma			
LP	‘B’	EMA	reactive*
NS (classic)	-	CD15, 30	reactive*
T lymphoblastic L	T CDc3,7,4+8,Tdt ----------		

Taylor CR
AIMM 2009



diffuse

Single
Cell type



B

T

CD19, CD20,
CD79a, Pax5
CD10, bcl 6,
MUM1
~~**Bcl 2,**~~
cyclinD1,
K,L
CD23
(cd5,cd43)

Small cell
V
large cell

CD3
CD5,CD43
CD4,CD8,
CD7
CD56

B cell -Diffuse lymphoma Phenotypes

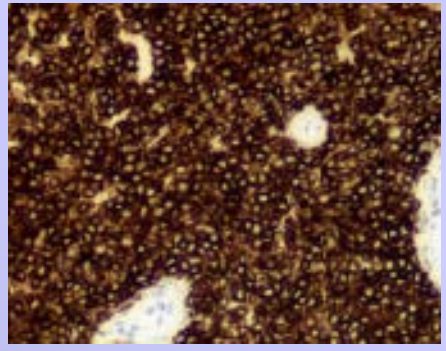
CD s	B*	10	21	23	5	43	bcl6	other*
B								
SL lymph/CLL	+			+	+	+		cd11c
L'pcytoid	+							CIg,cd38
FCC	+	+	(+/-)	-/+			+	(bcl2)
mantle	+				+	+		D1
marginal	+		[+/-]			-/+		OCT,BOB
Diff large cell	+	+/-				-/+	+/-	+/-MUM1
Burkitt	+	+				-/+	+	cd38
T -most are CD2+,3 +					+	+		

*CD19, 20, 22, 79a, Pax5

[ ] FDC network

Adapted fr Taylor et al. Immunomicroscopy and Molecular Morphology Elsevier/Saunders. 2005.

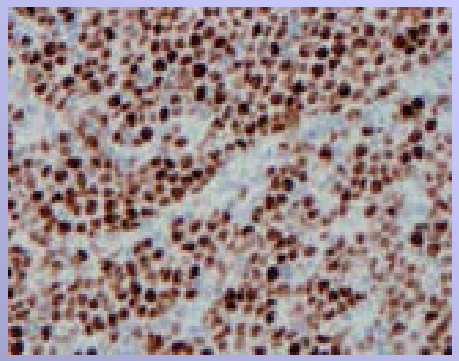
DLBCL



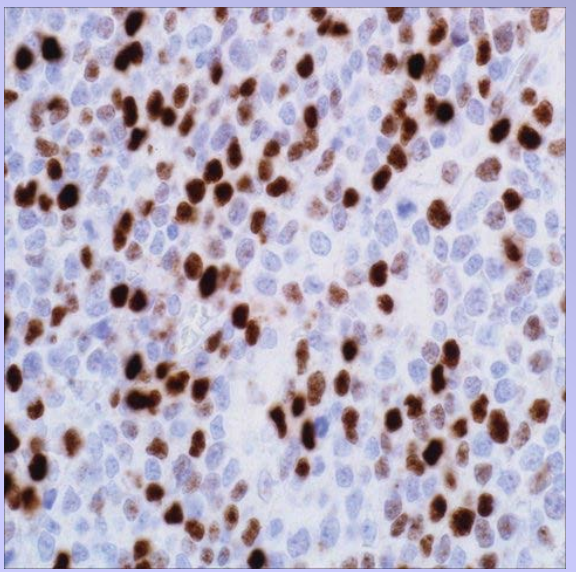
CD 20

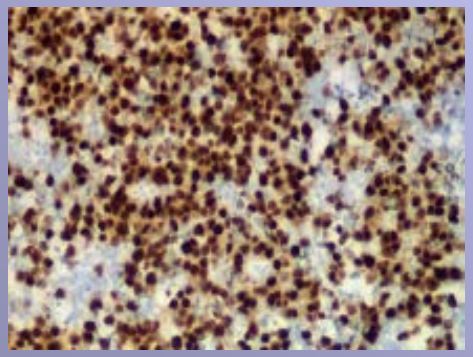
Post or non GC case –

Poorer Prognosis?



Bcl 6



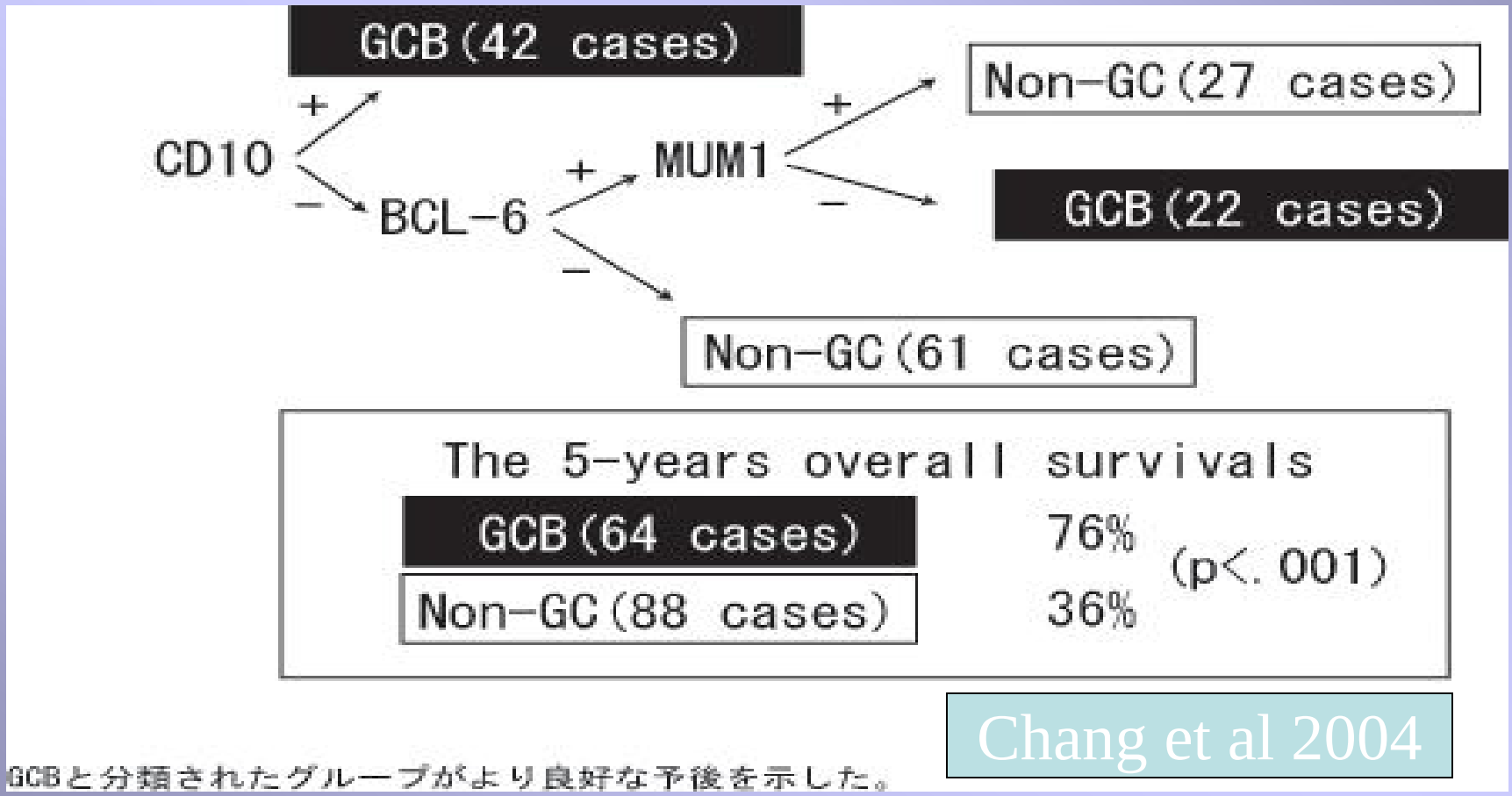


MUM 1

Myc/BCL2 both positive
also indicates poor prognosis
Threshold >40% myc+

Germinal Center GC - and Post GC - DLBCL

GC = CD10+, or BCL6+ and MUM -



DLBCL..Also….Bcl2+ and survivin + = poorer prognosis

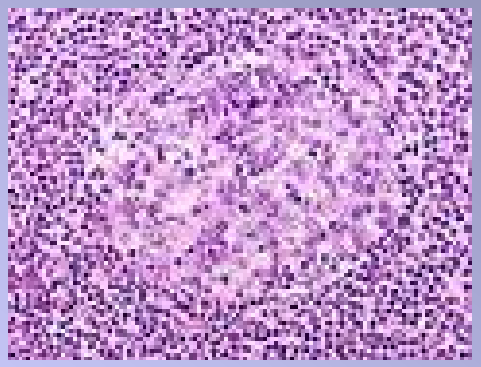
CYCLIN D1 / PRAD 1 : MANTLE C L.

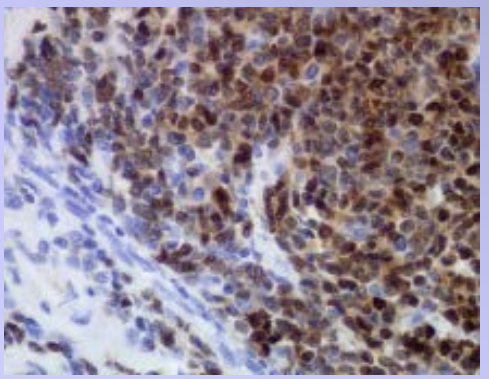
T 11;14, translocates BCL-1

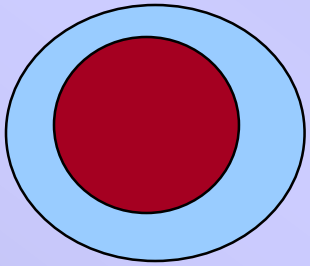
MCL 90% +

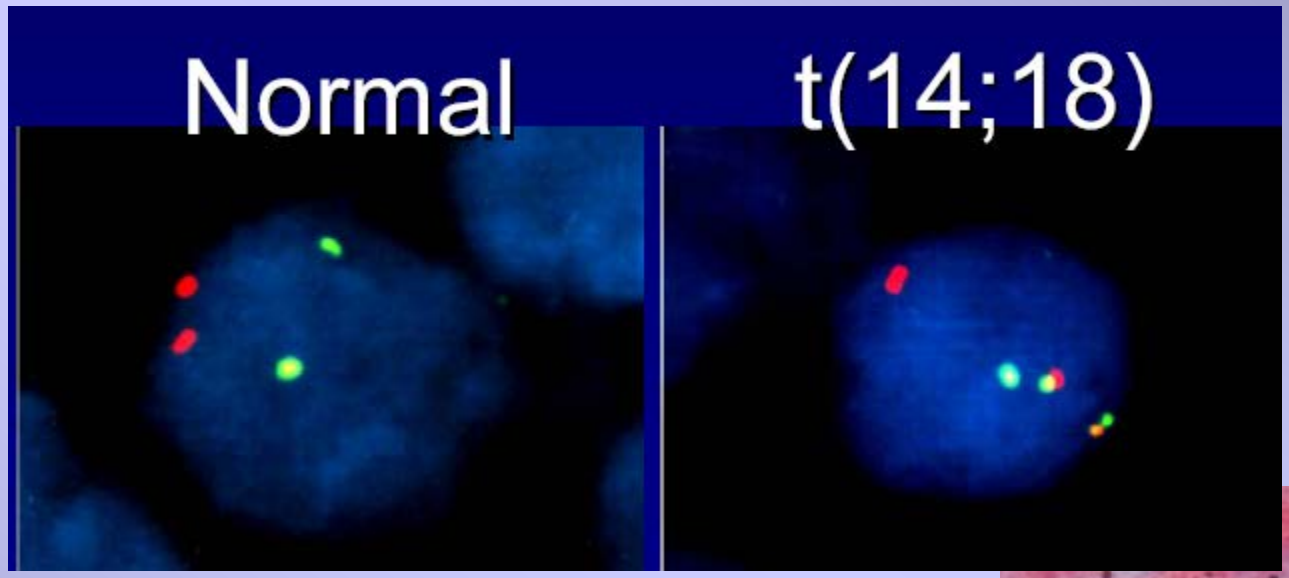
Other ML -:
rare immcytoma; marginal ML

Nuclear stain; **requires AR ++***

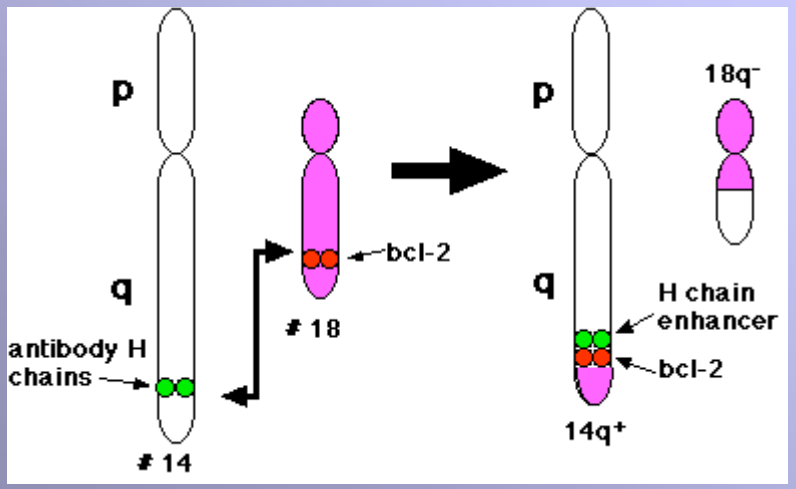


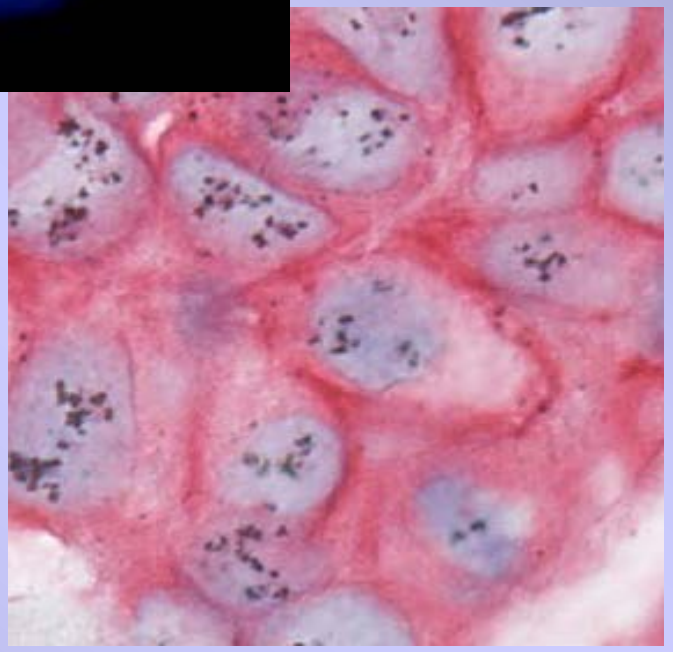






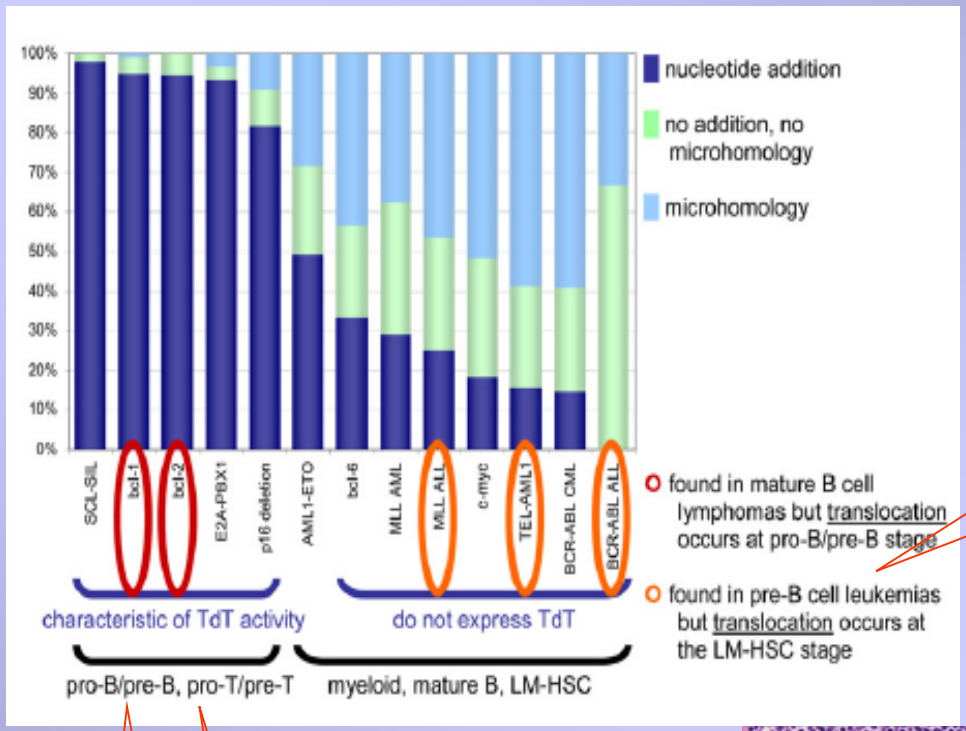
FISH Surti 2003





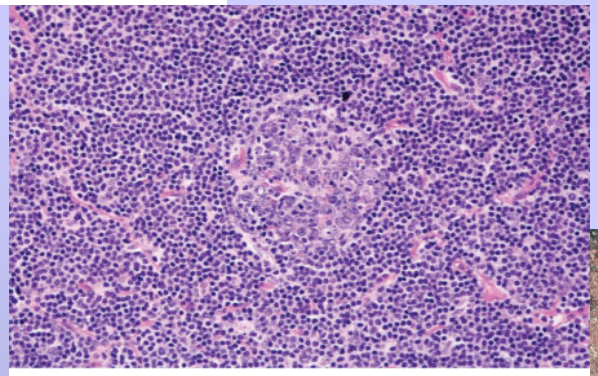
Goldfish -Tubbs 2001

Tsai et al. USC



Seen in 'mature' B lymphomas' but break at early B stage 'cancer stem cell'

Bcl-1 ---------- **Mantle cell**



Source: Lichtman MA, Shafer MS, Felgar RE, Wang N: *Lichtman's Atlas of Hematology*: http://www.accessmedicine.com
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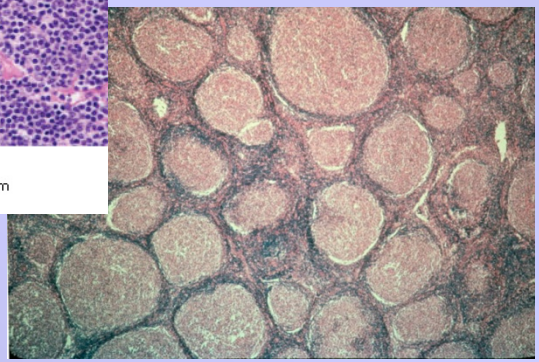
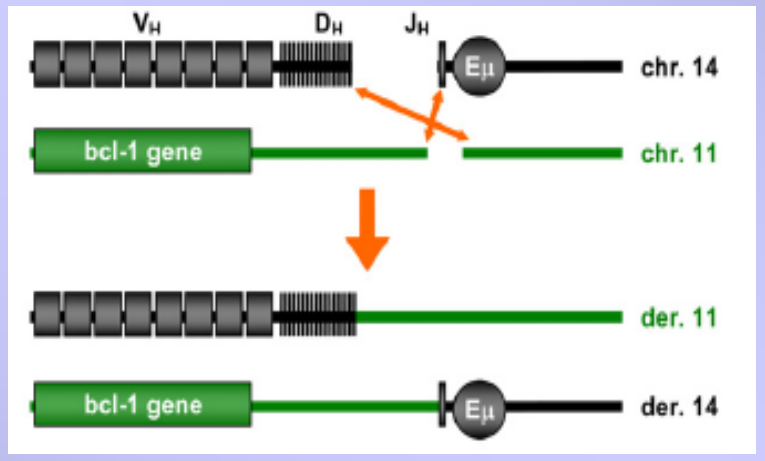
Bcl-2 ---------- **Follicular center cell**

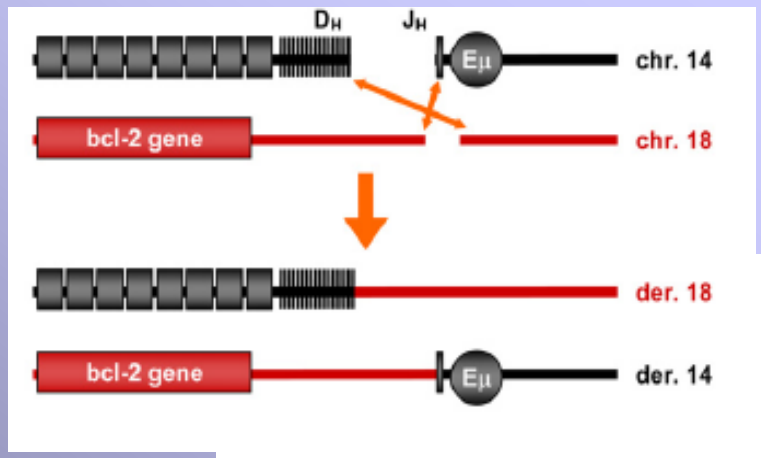


Tsai et al

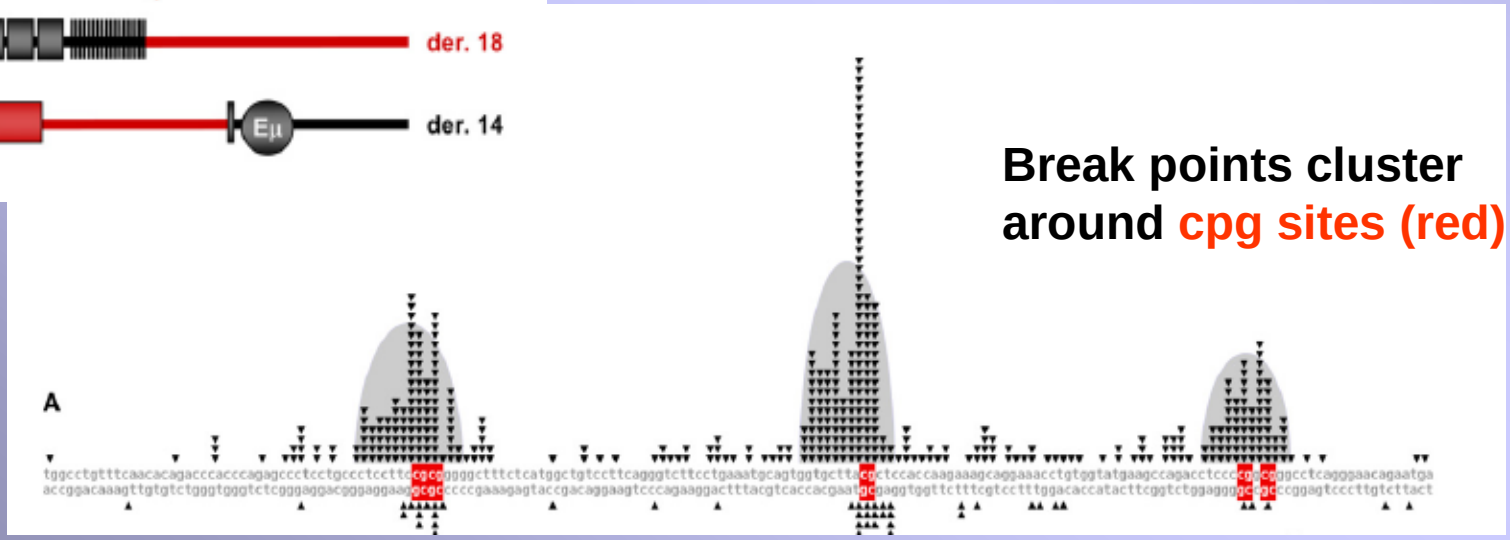


Bcl-1 - t(14;11) – mantle cell –B lymphoma

Translocation events common in ML
Because of gene rearrangement



Bcl-2 - t(14;18) – follicular center cell –B lymphoma



Break points cluster around cpg sites (red)

Lymphomas - remarkable fit between ‘old morphologic types
And IHC and molecular classification

t (14;18)	FCC	bcl-2
t (11;14)	mantle	bcl-1;cycD1
t (2;5)	ALCL	npm/alk
t(11;18)	marginal(malt)	**API2/MALT1**
t(9;14)	lymphoplasma	pax5
t (8;14)	burkitt	myc
t (3;14)/n 12+	diff large cell	bcl-6
	CLL	

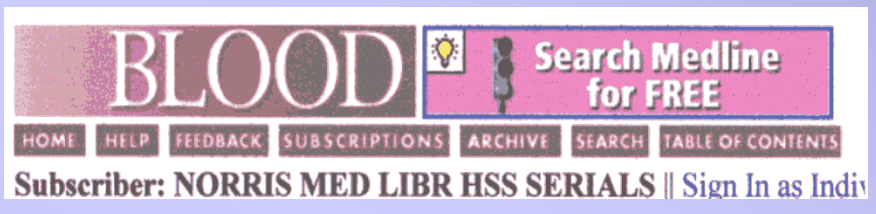
T cell - Diffuse lymphoma Phenotypes

CD s	2,3	4	8	5	7	25	30	56	other
B				-/+					
T.									
NK	+#		-/+			+		+	GrB,Fas
Adult T	+	+		+		+	-/+		FOXP3
Entero Ass	+		-/+		+	-/+	-/+	-/+	GrB, 103
M fungoides	+	+	-/+	+					
Peripheral	+	+	-/+	-/+	-/+		-/+		
Anaplastic	-/+	-/+	-/+	-/+	-/+	+	+		GrB,EMA
Lymphoblastic*	+	-/+	-/+	-/+	-/+				cd10

*+CD99,34

cytoplasmic CD3 only

CRT 2017

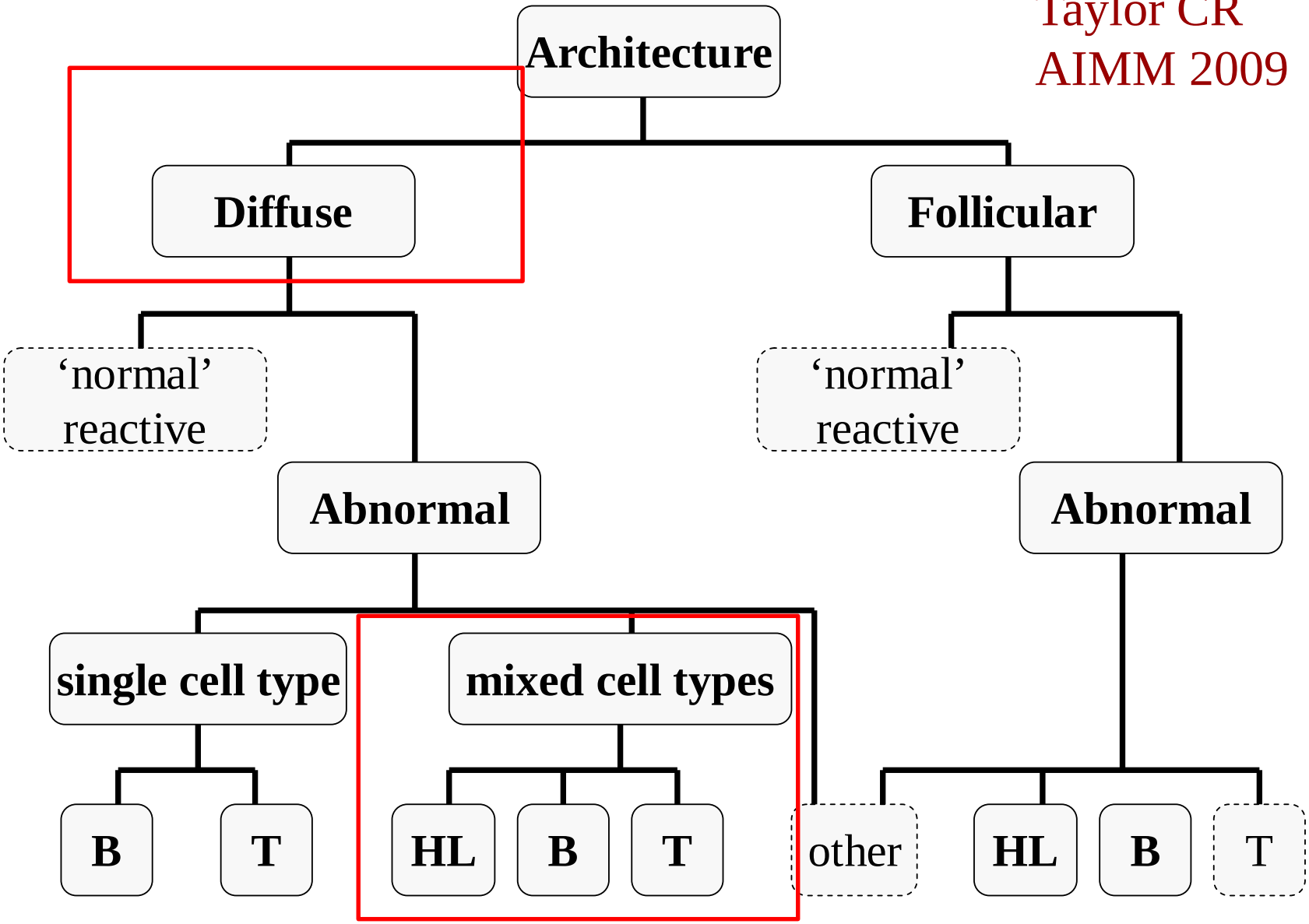


89, 3909, 97

Expert agreement with consensus

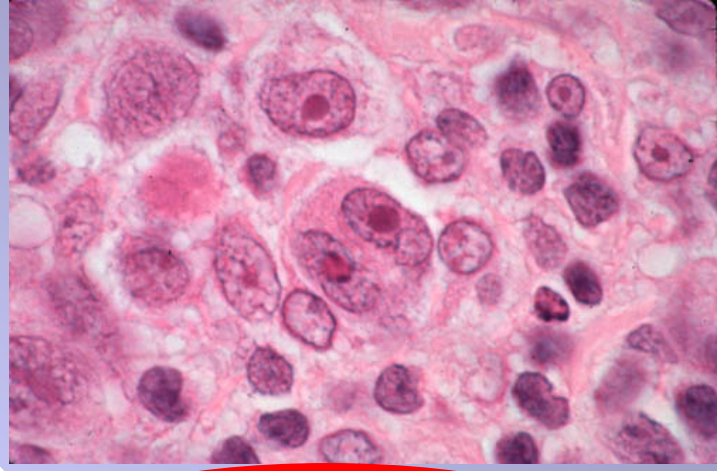
	Histology	+ IHC
Follicular - (by grade)	93 (60)	94 (61)
MALT / marginal z	84	86
small lymph / CLL	84	87
lymphoplasmacytoid	53	56
Burkitt (like)	47	53
mantle	77	87
diff Large B	73	87
precursor T	52	89
peripheral T	45	86
anaplastic large T/null	46	85

Taylor CR
AIMM 2009



Diffuse

Mixed



B

Histio + Dendritic

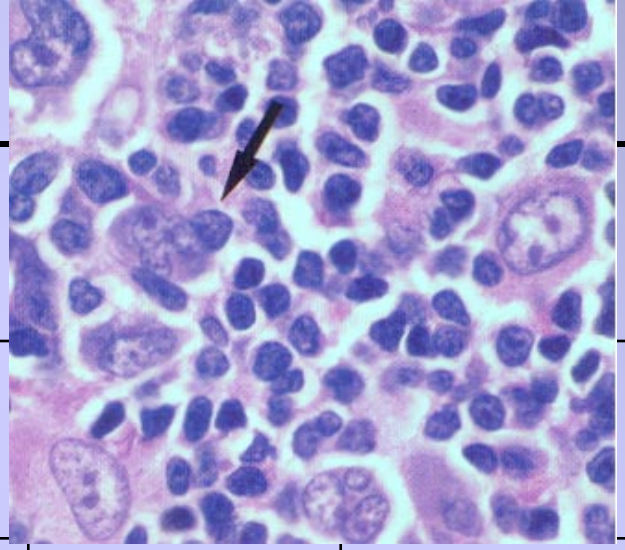
T

Hodgkin L

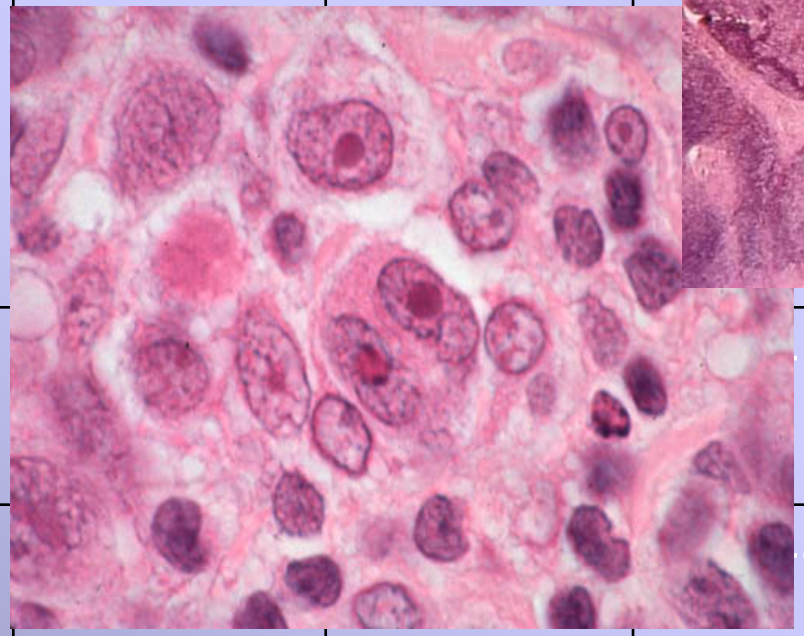
CD19, CD20, CD79a, CD10, BCL6, MUM 1 Cyclin D1, K,L CD23 (CD5,CD43)

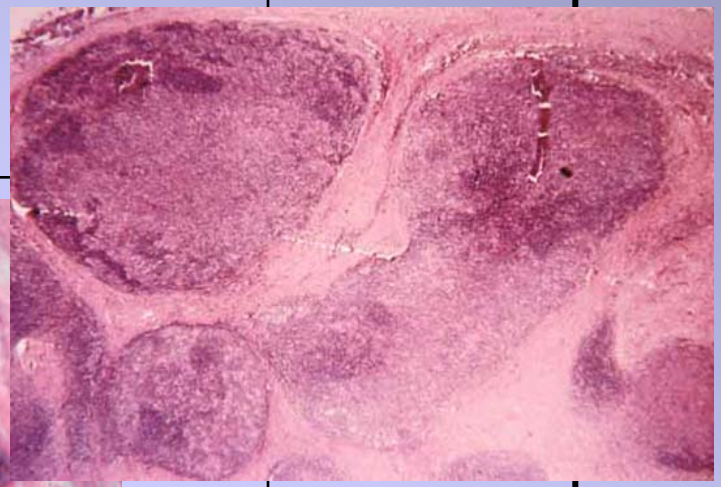
CD3 CD5, CD43 CD4, CD8, CD7, CD25, CD56 [CD30] [ALK]

(CD45) (EMA) CD30, CD15 BLA36, Fascin MUM1 Pax5 CD40 LMP



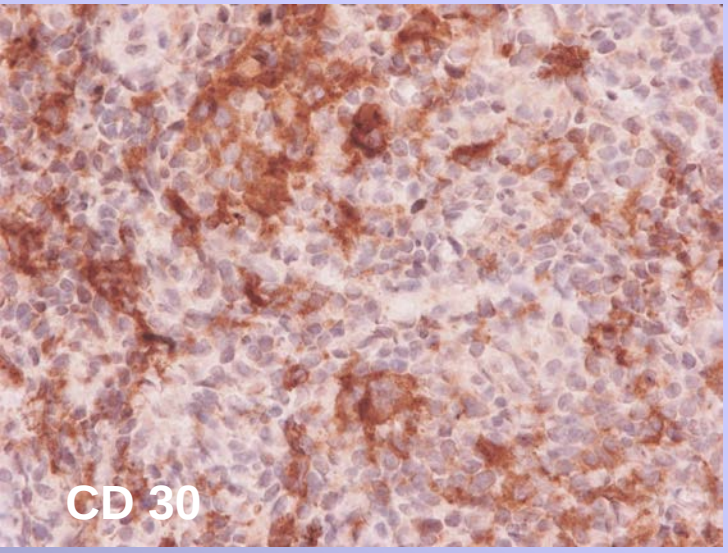
			R-S cells	other
LP				
Classical MC LR				
NS				Fib bands
LD			+	

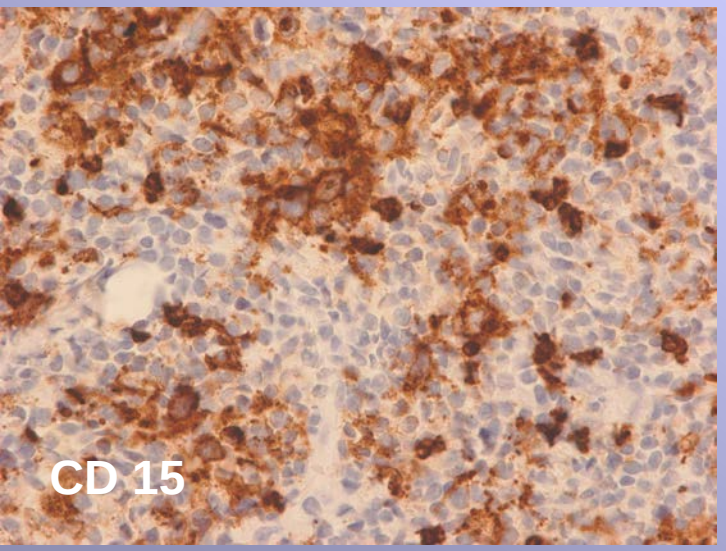


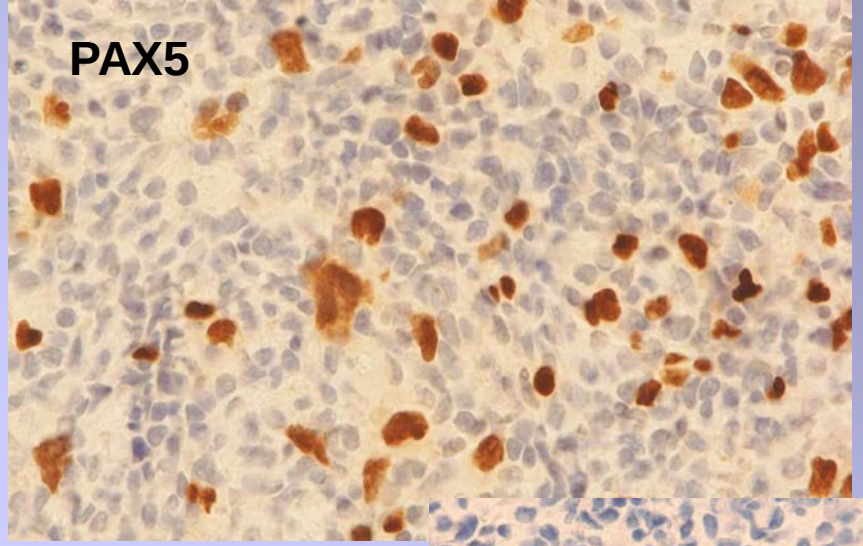


Classic HL

diffuse

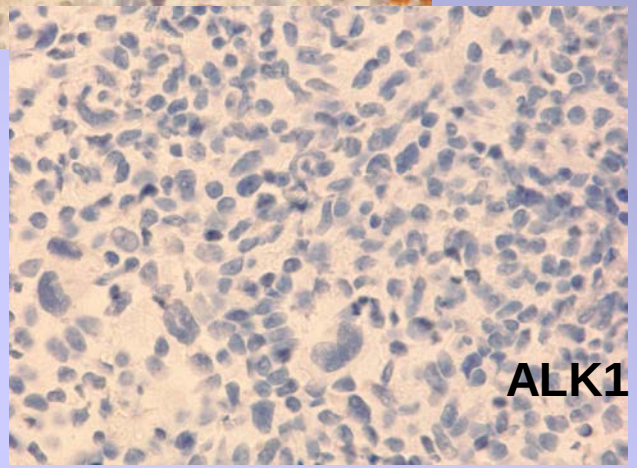






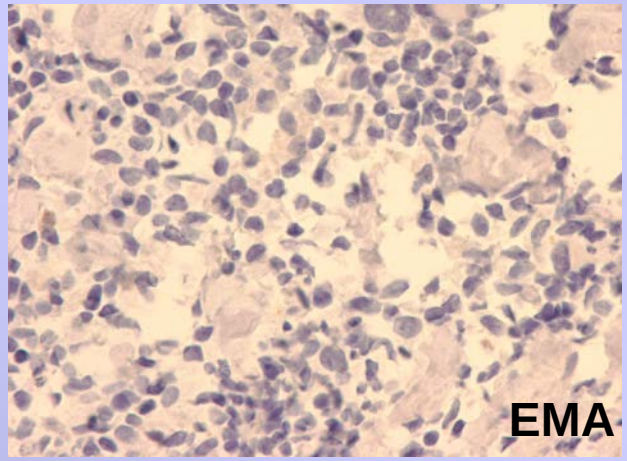
vs

ALCL +

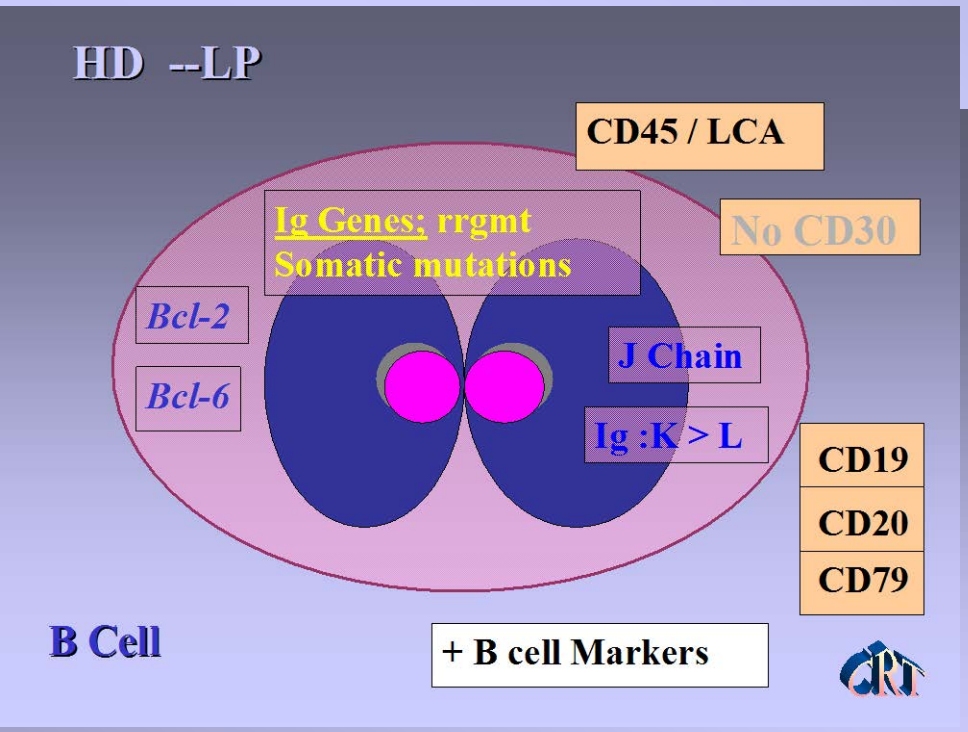


vs

HL LP+

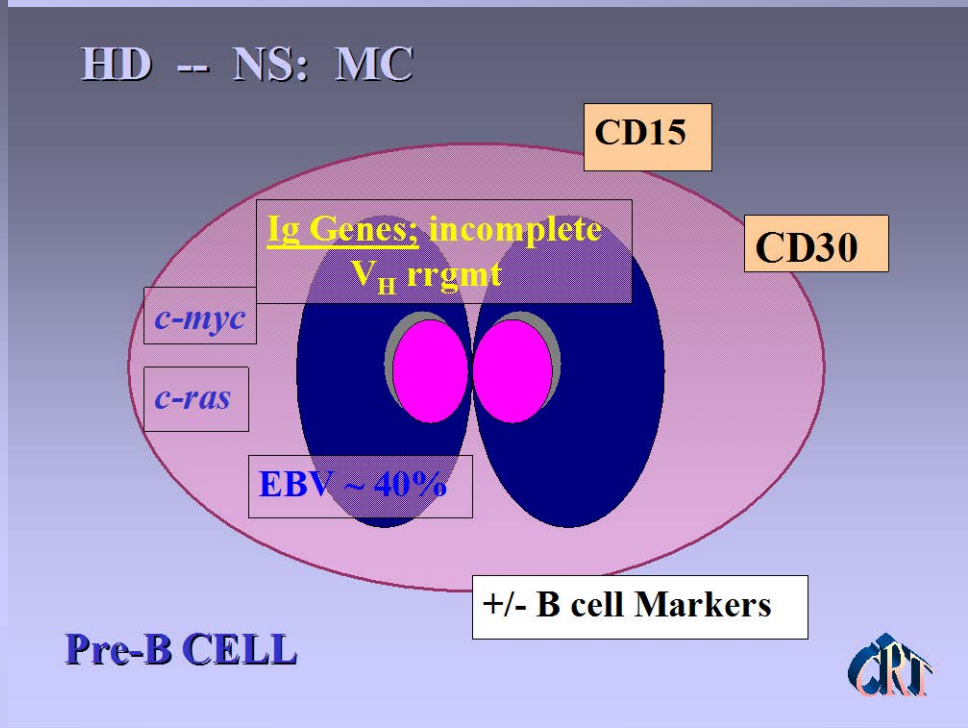


Markers useful for subclass HL and other lymphomas



HDLP - CD 20, CD45

HD classical CD 15, CD30



ELSEVIER

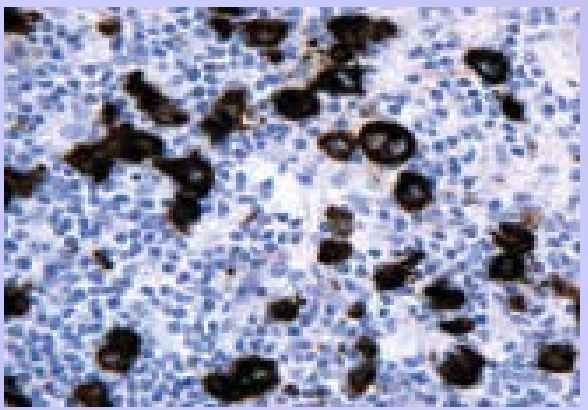
Taylor CR
Human Path 36, 1-4, 2005.

Human PATHOLOGY
www.elsevier.com/locate/humpath

Editorial

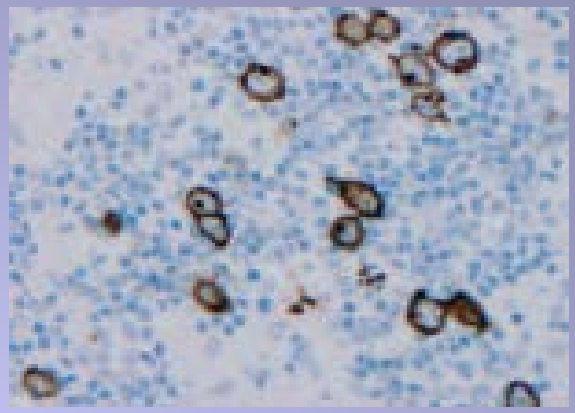
Hodgkin's disease is a non-hodgkin lymphoma

Taylor, Riley, AIMM 9,187,2001



CD 15

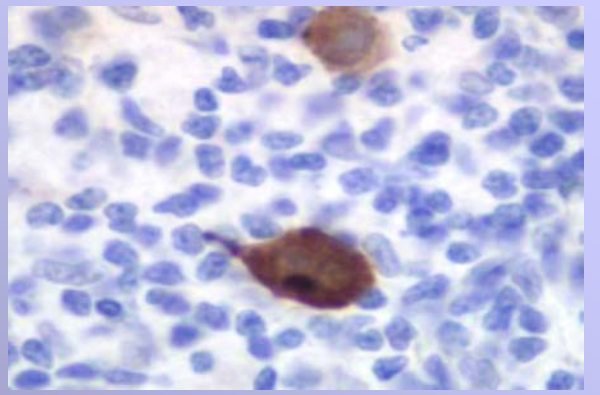
CD 30



HODGKIN

CLASSIC

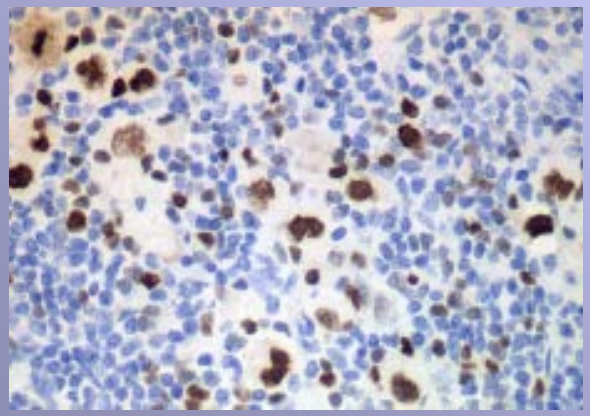
MC



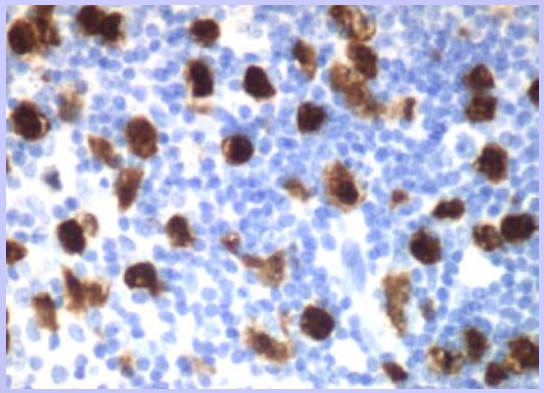
LMP

ALCL

ALK



MUM 1



CHL v ALCL.

CD30	90+%	100%
T ags	0-30%	20-80%
B ags	10-60%	0-30%
CD15	90%	0-25%
CD45	10%	30-90%
EMA	10-20%	30-60%
Pax5	90-95%	-
ALK	-	80-90%*
Clusterin	-	80%

*not cutaneous ALCL

Weshi et al Leuk Lymphoma 48, 1764, 2007

HL vs T cell (histiocyte) rich B cell lymphoma

Table I. Referral diagnosis of 61 TC/HRBCL cases.

Diagnosis	No. of cases
Classic Hodgkin's disease	20
cHL, lymphocyte – predominant	12
cHL, mixed cellularity	7
cHL, nodular sclerosis	1
Nodular, lymphocyte – predominant HL	5
Non-Hodgkin's lymphoma	25
TCRBCL	11
Diffuse mixed B cell lymphoma	8
Peripheral T-cell lymphoma	4
Diffuse large B cell lymphoma	2
Lymphoproliferative disorder	7
Malignant lymphoma NOS *vs.* HL	4

CD20, CD79a, CD15, Fascin, EMA

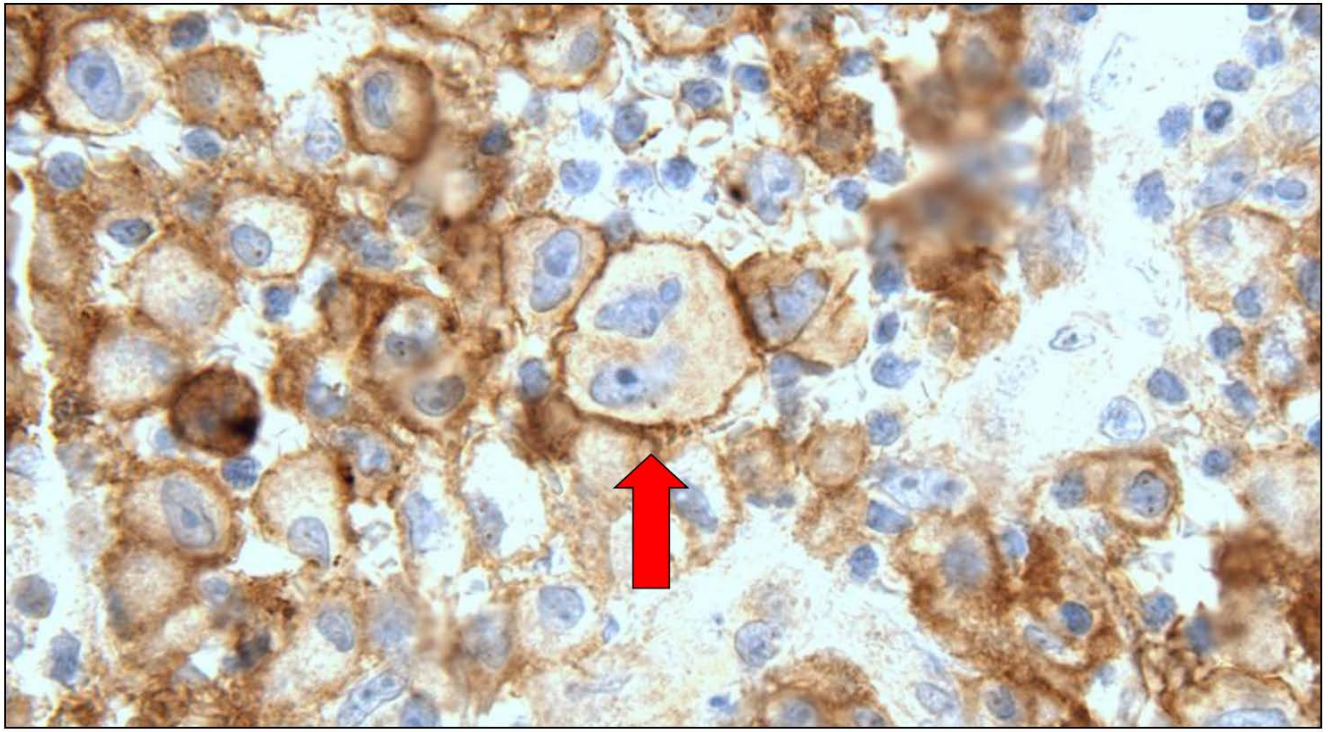
PANEL	**Nod LP** **RS cell**	**Classic** **RS cell**	**LRBcell** **Large cell**	**ALCL** **Large cell**
cd45	**+**		**+**	**-/+**
cd30		**+**		**+**
cd15		**+**		
cd20,79a	**+**	**-/+**	**+**	
MUM1		**+**	**-/+**	
Bcl6	**+**	**-/+**	**+**	
Pax5	**+**	**+**	**+**	
OCT2	**+**		**+**	
EMA	**+/-**	**+**	**-/+**	**+/-**
lymphocytes	manyB+T	Vary B+T	Many B	few

IHC

Large Cells

Added to which is the PD-1 PD L-1 story, which now is becoming important for lymphomas
-----With all of the challenges of scoring etc.

PD-L1 Expression in Primary CHL



1. 87% (33 of 38 cases) of primary CHL show PD-L1 expression by the Reed-Sternberg cells

Chen BJ et al., Clin Cancer Res., 2013

Nivolumab in Relapsed/ Refractory CHL

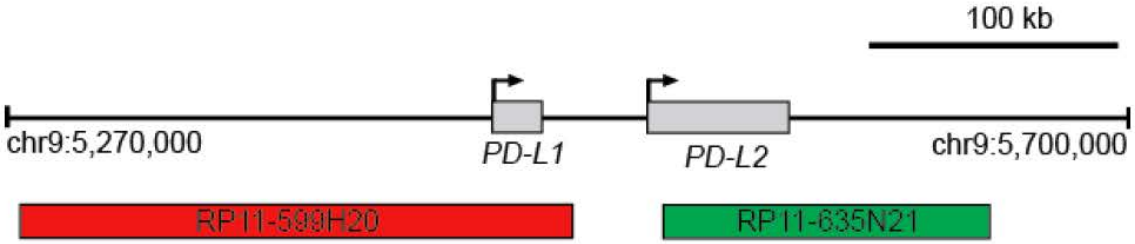
1. PD-L1/2 locus integrity

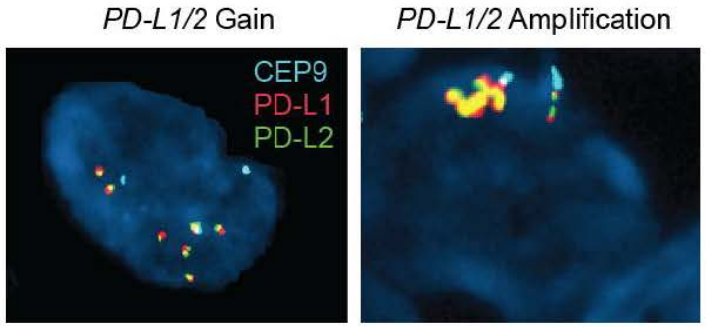
Red=PD-L1

Green=PD-L2

Yellow= Red + Green

Cyan=Centromere

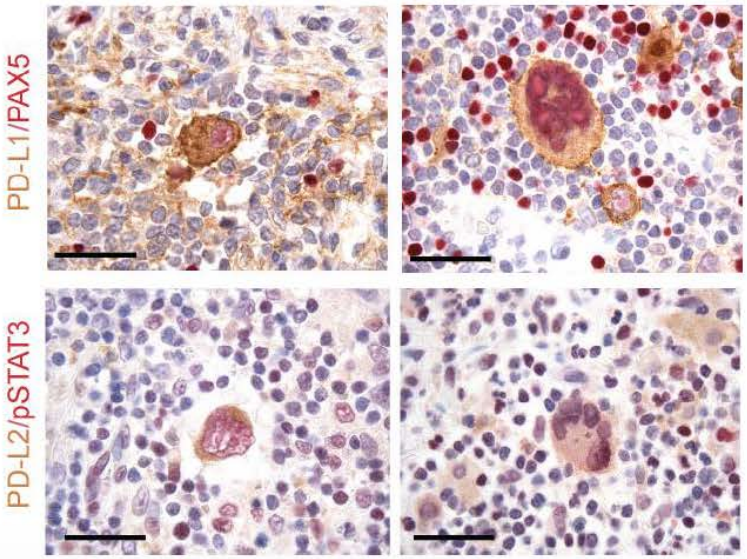




2. PD-L1/2 Protein Expression

PD-L1 (brown)
PAX-5 (red)

PD-L2 (brown)
pSTAT3 (red)

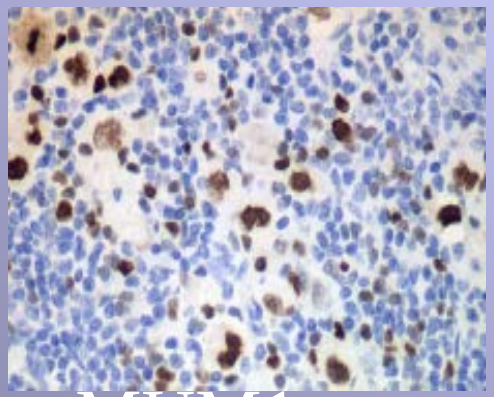


Ansell SM et al.. N Engl J Med 2014

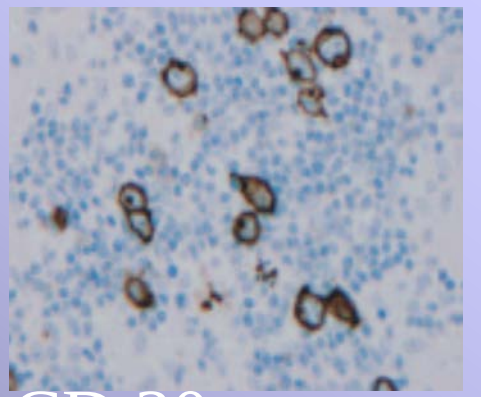
My own interest

Taylor Lancet 1974

The Nature of Reed Sternberg Cells



MUM1



CD 30

Reprinted from THE LANCET, *October* 5, 1974, *pp.* 802-807

THE NATURE OF REED-STERNBERG CELLS AND OTHER MALIGNANT "RETICULUM" CELLS

CLIVE R. TAYLOR

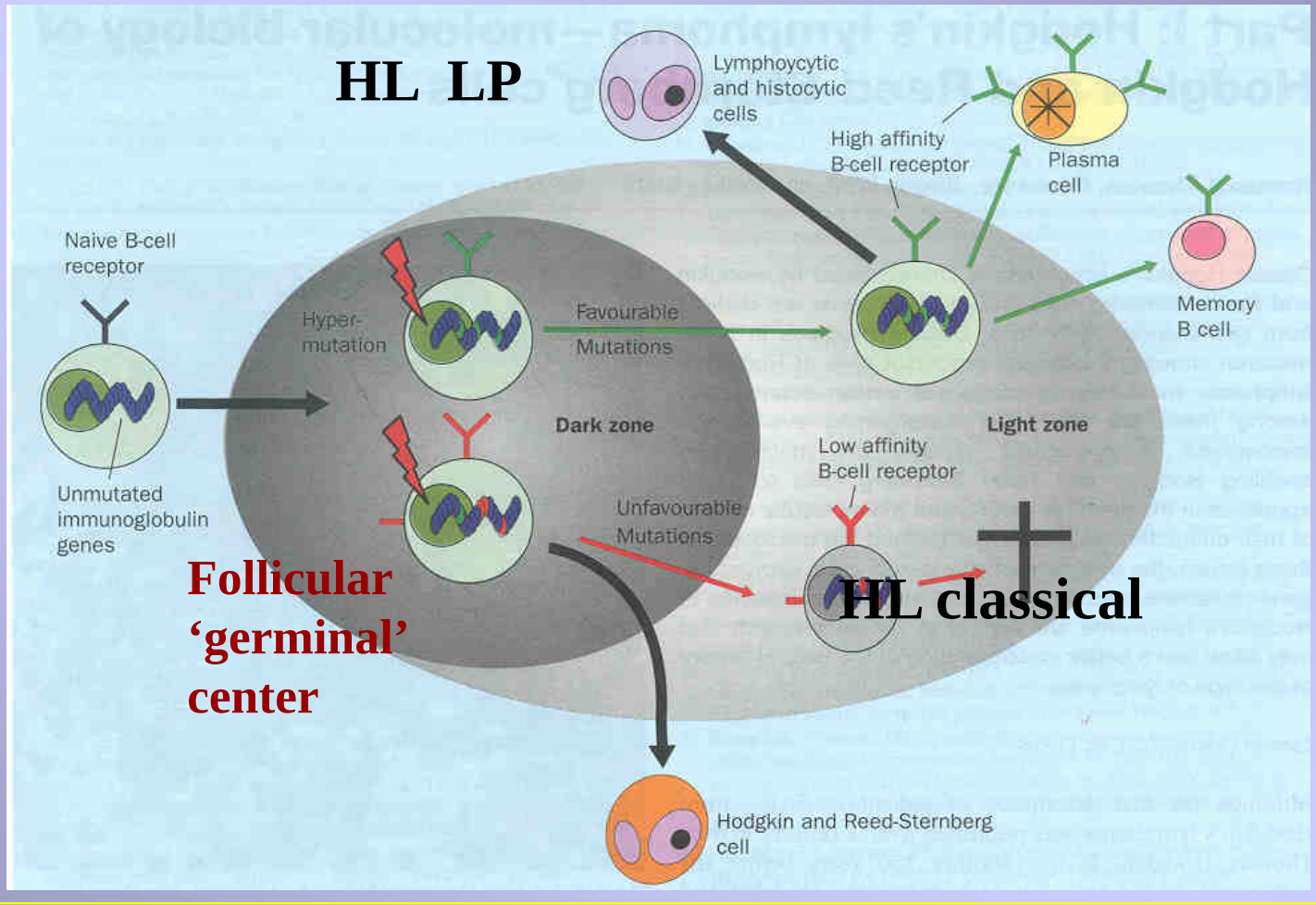
Gibson Laboratories, Radcliffe Infirmary, Oxford

Summary Immunoperoxidase methods have been applied to formalin-paraffin sections of more than 100 lymphoreticular neoplasms. Intracellular immunoglobulin components have been identified in plasma-cell neoplasms, and also in the "malignant reticulum cells" of some cases of reticulosarcoma and Hodgkin's disease. Some of the preliminary morphological correlations are presented, and the significance of these findings is briefly considered. Finally, a tentative scheme is offered, relating some of the different histological types of lymphoreticular neoplasm to the various morphological forms assumed by the lymphocyte during its cell cycle.

Introduction

MANY of the problems of diagnosis and classification of lymphoreticular neoplasms stem from the lack of a clear understanding of the basic cell types from which these neoplasms originate. In particular, there is the problem of those neoplasms which are traditionally believed to be derived from the "reticulum cell"—principally Hodgkin's disease and the "reticulum cell sarcoma" group (the histiocytic and stem-cell lymphomas of the American literature [1]).

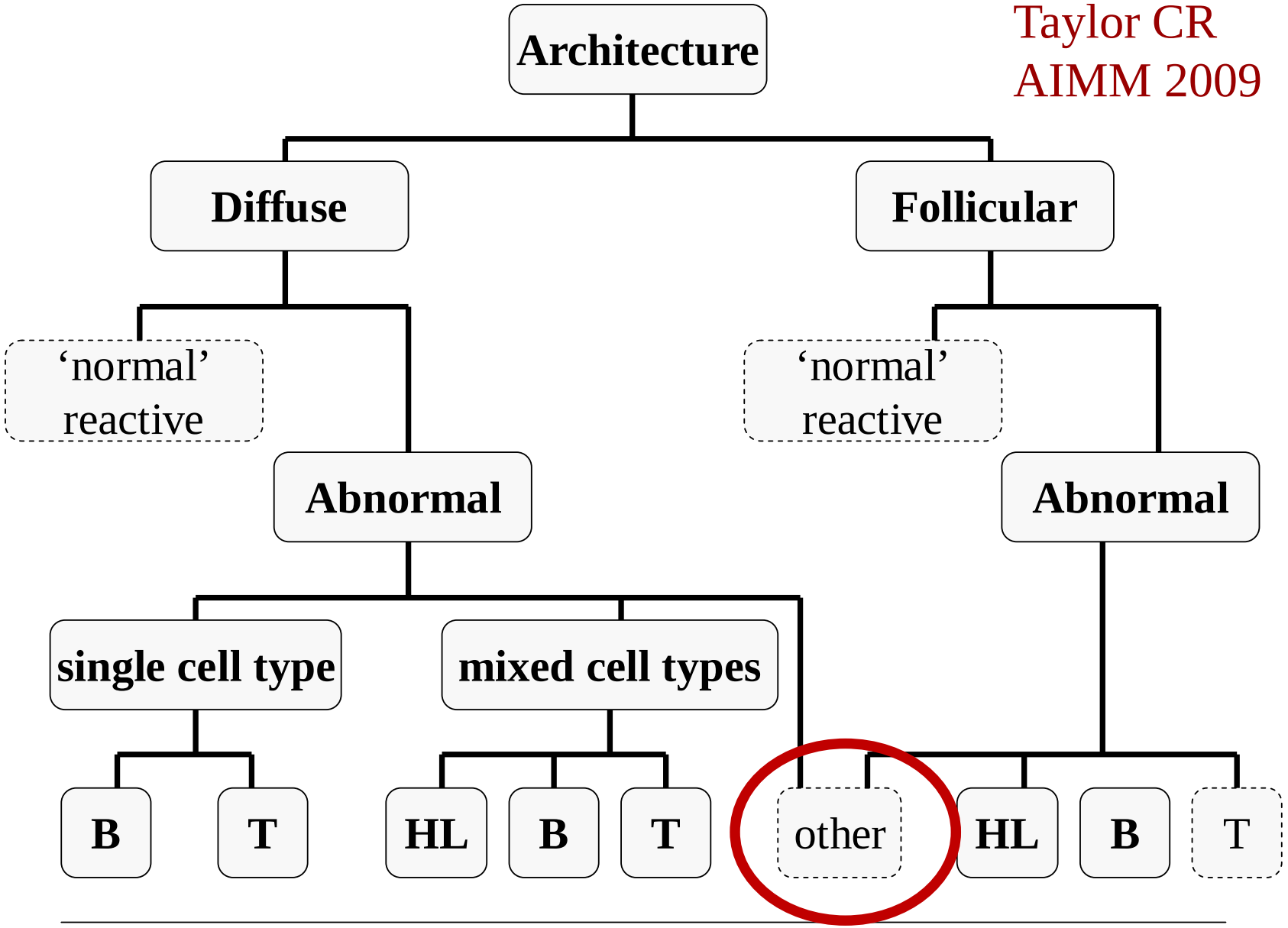
Immunoglobulin has been identified within Reed-Sternberg cells [2,3] and within the cells of some cases of reticulum-cell sarcoma [4] by the application of a peroxidase-labelled antibody method to formalin-fixed paraffin-embedded tissue. I have confirmed and consolidated these observations in cases of Hodgkin's disease, reticulum-cell sarcoma, and follicular lymphoma. This evidence supports the suggestion that at least some so-called "malignant reticulum cells"



Molecular Biology of Hodgkin's Lymphoma –

Thomas et al – Lancet Oncology 5, 11, 2004

Taylor CR
AIMM 2009



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Part I. *Appl. Immunohistochem & Mol Morphol, 17 :366-374, 2009.*
Part II. *Appl. Immunohistochem & Mol Morphol, 17 :470-482, 2009.*

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Geller SJ, Taylor CR. Hodgkin; the Man and his Disease. Virchow Arch 460. DOI 10.1007/s00428-013-1442-0. 2013

Van den Tweel, J, Gu, J, Taylor CR. From Magic to Molecules: An Illustrated History of Disease. Beijing University Press, 2016. Amazon.com