



**HOT  
NEWS**

**IN HEMATOLOGY**

Sindromi  
linfoproliferative  
ed oltre...

## **OTTIMIZZAZIONE DIAGNOSTICA**

**Stefano A. Pileri**

**MILANO**

**27 Aprile 2022**

HILTON MILAN

## Disclosures of Stefano A. Pileri

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
BeiGene						X	
Takeda						X	
Roche					X		
Diatech						X	

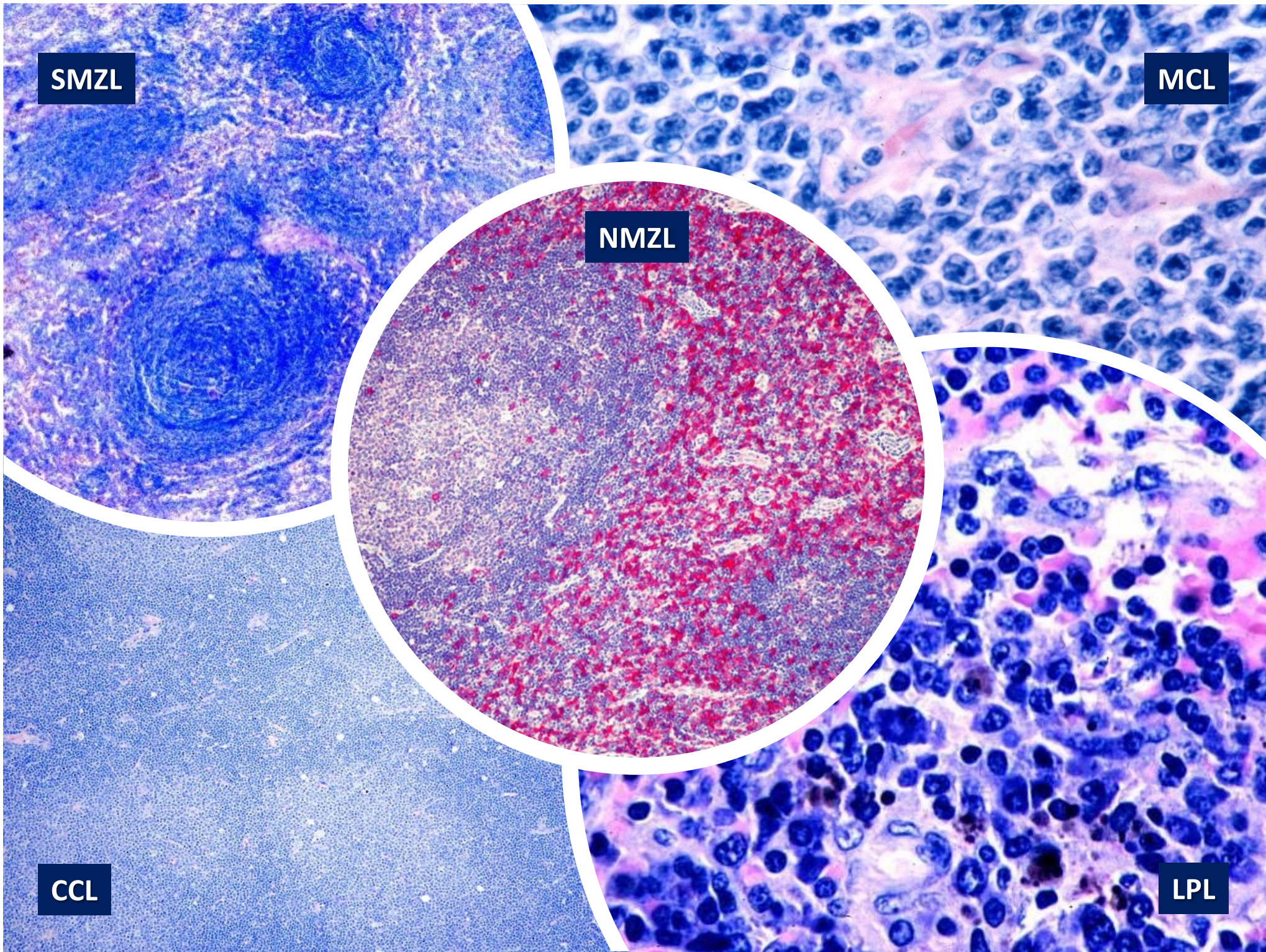
SMZL

MCL

NMZL

CCL

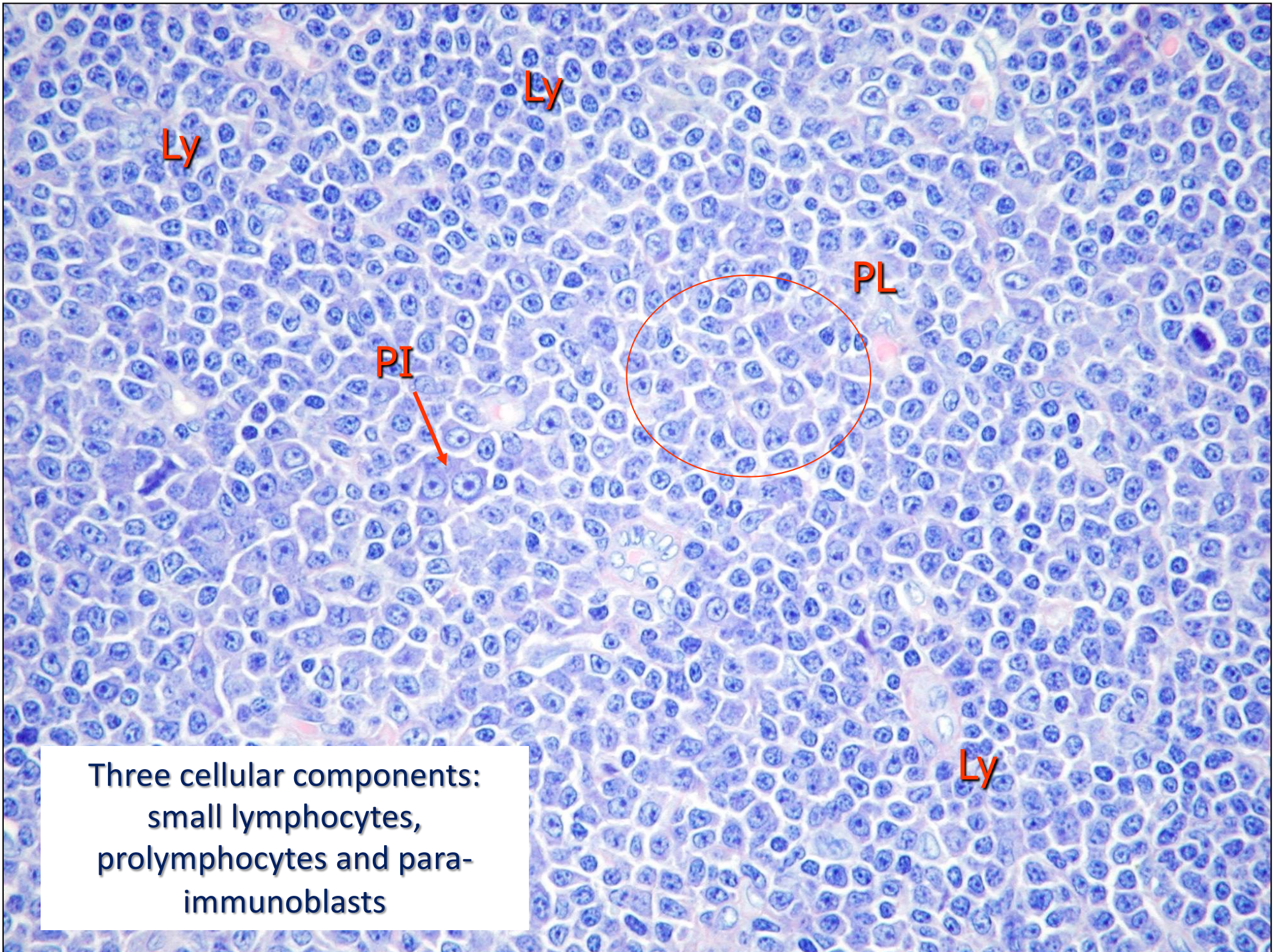
LPL



## **Chronic lymphocytic leukaemia/ small lymphocytic lymphoma**

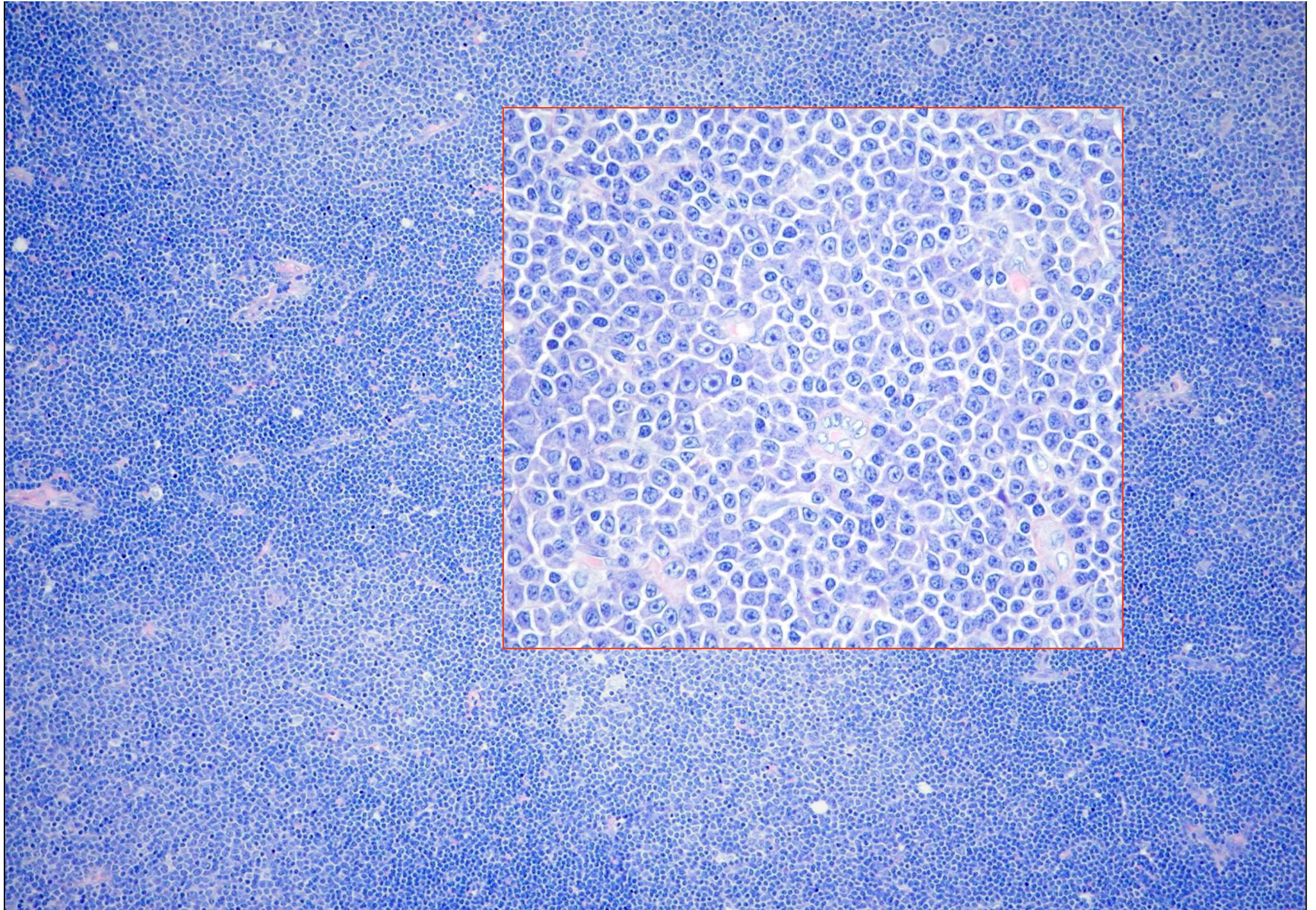
### **Definition**

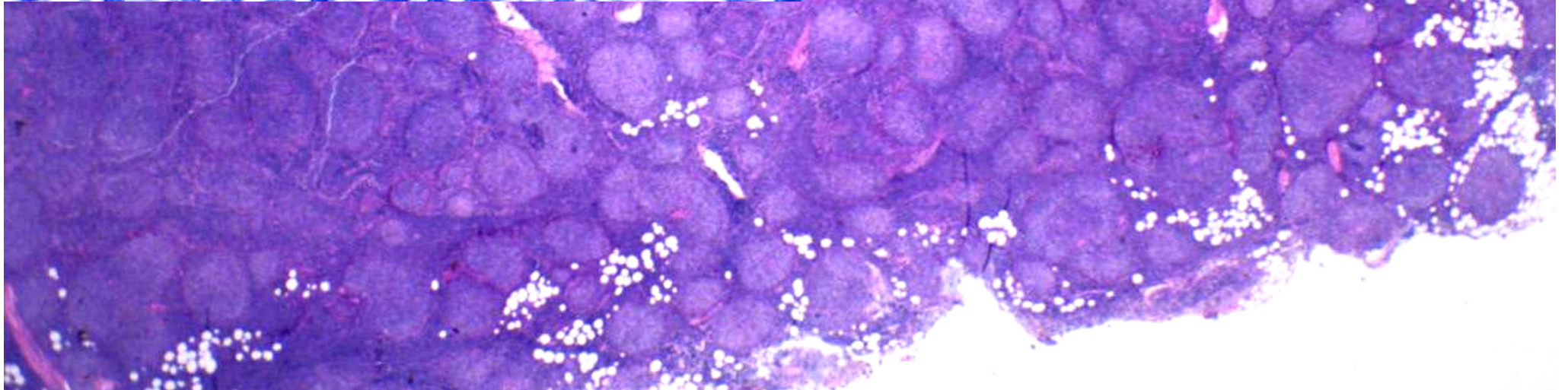
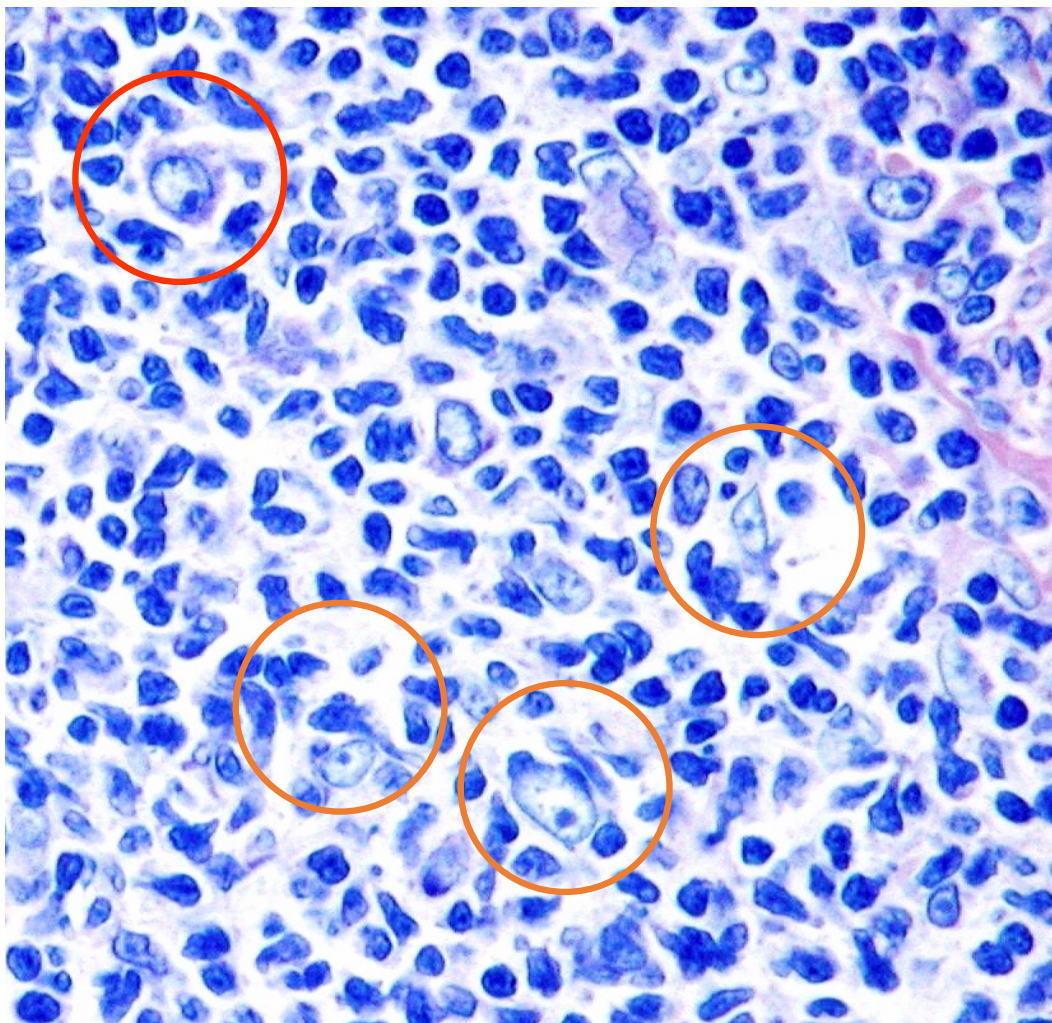
Chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) is a neoplasm composed of monomorphic small mature B cells that coexpress CD5 and CD23. There must be a monoclonal B-cell count  $\geq 5 \times 10^9/L$ , with the characteristic morphology and phenotype of CLL in the peripheral blood. Individuals with a clonal CLL-like cell count  $< 5 \times 10^9/L$  and without lymphadenopathy, organomegaly, or other extramedullary disease are considered to have monoclonal B-cell lymphocytosis. Although CLL and SLL are the same disease, the term SLL is used for cases with a circulating CLL cell count  $< 5 \times 10^9/L$  and documented nodal, splenic, or other extramedullary involvement {1523}.



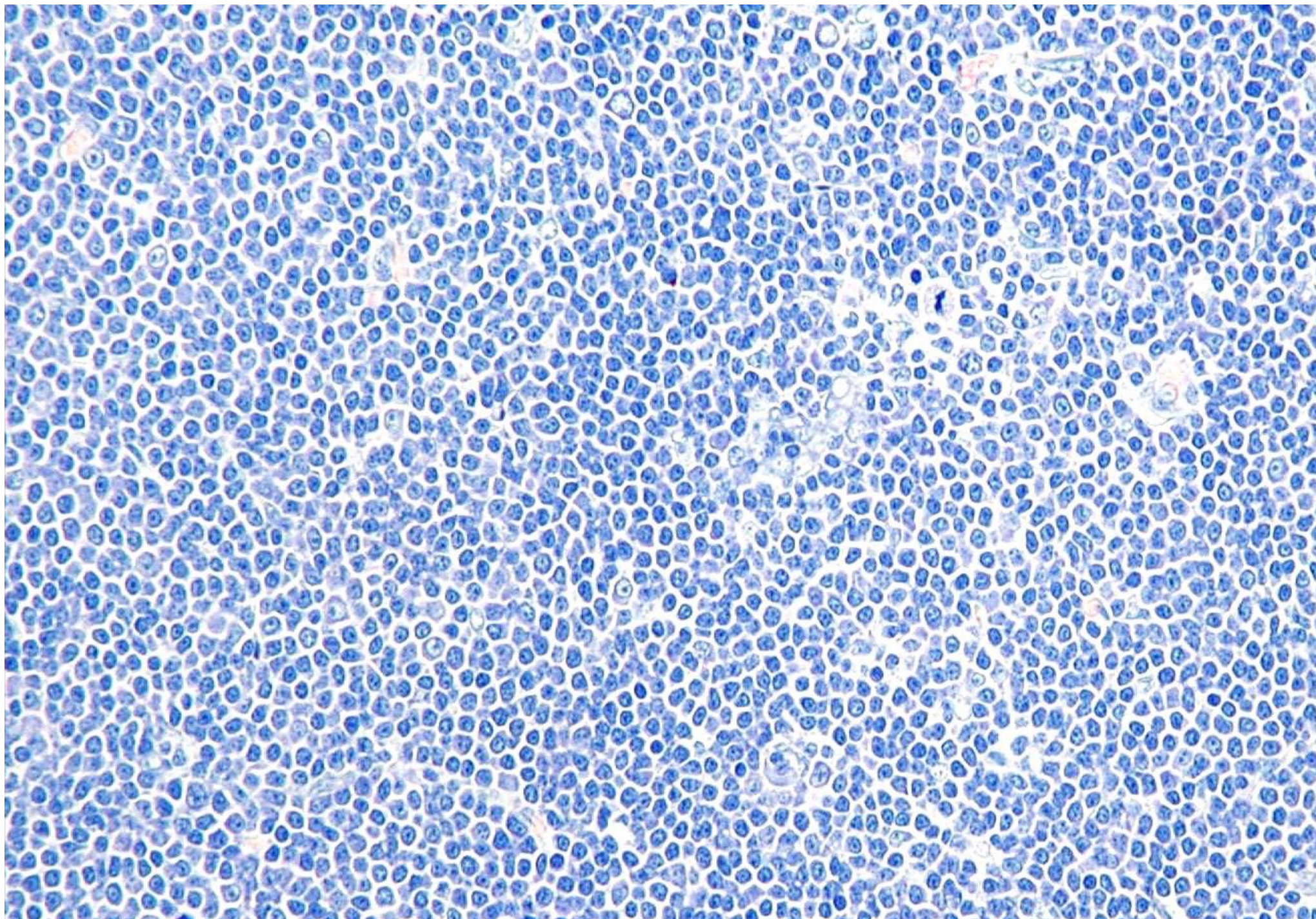
Three cellular components:  
small lymphocytes,  
prolymphocytes and para-  
immunoblasts

Pseudo-follicular pattern: 85% of cases (lymph node, bone-marrow, extranodal sites)





Diffuse growth pattern: 7% of cases; scanty prolymphocytes and paraimmunoblasts

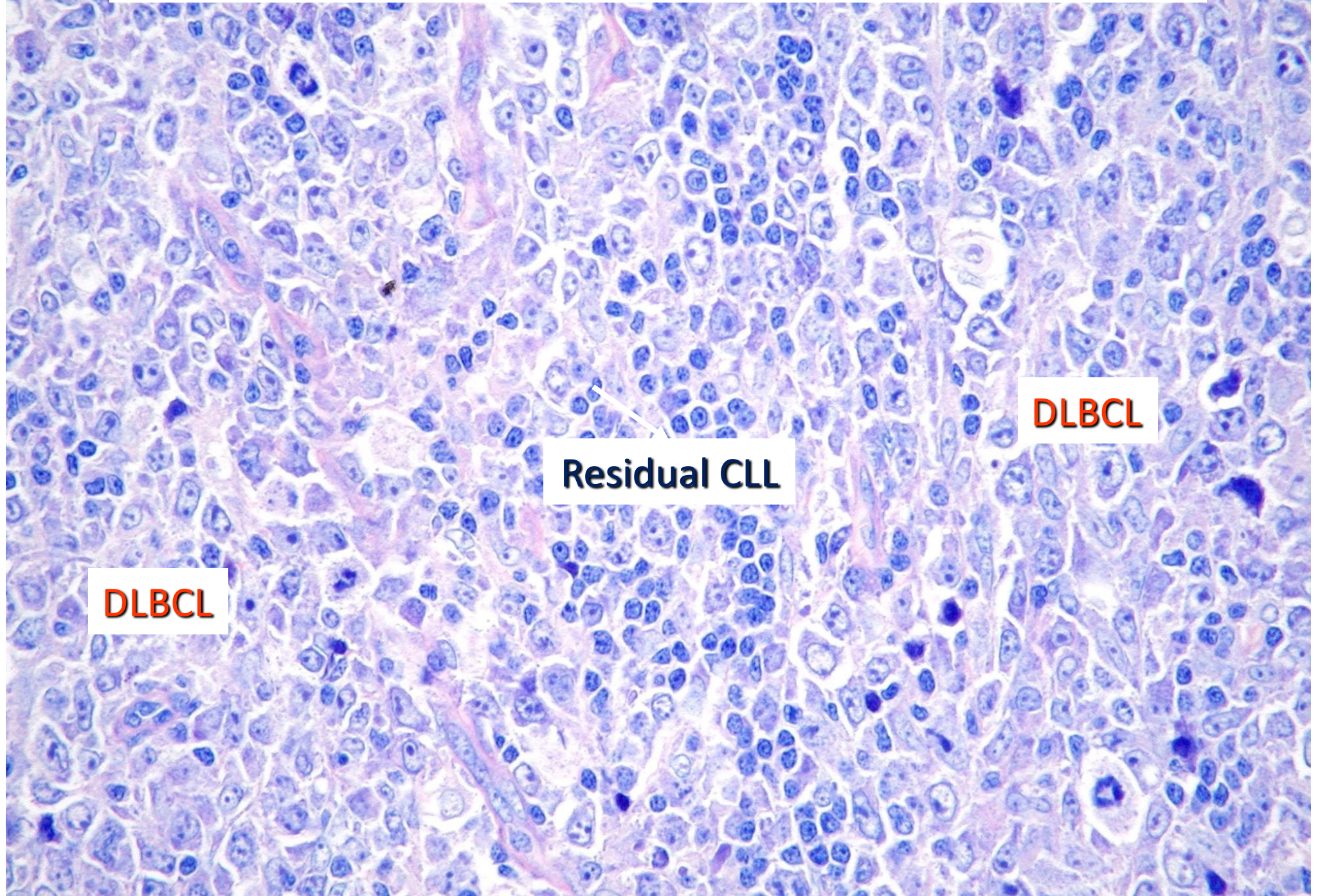




The image is a composite of two histological micrographs. The left half shows a tissue section stained with hematoxylin and eosin (H&E), displaying a dense population of cells with pink cytoplasm and purple nuclei. The right half shows a tissue section stained with hematoxylin (H), displaying a dense population of cells with purple nuclei and light blue cytoplasm. A white diamond shape is overlaid on the center of the image, containing the text "Tumor-forming".

Tumor-forming

Richter Syndrome – DLBCL type: related or unrelated (EBV+)

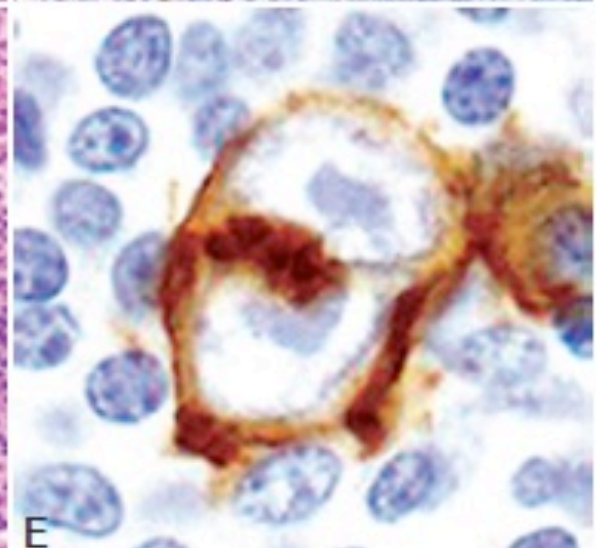
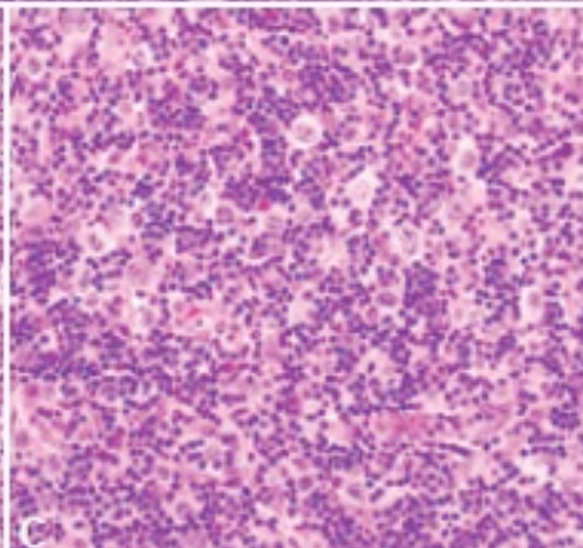
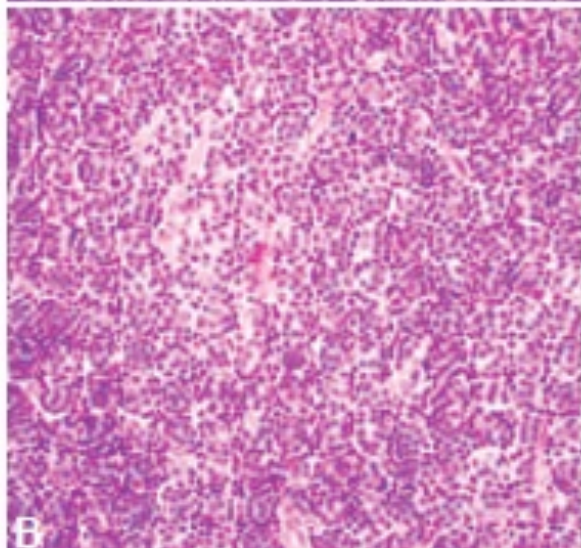
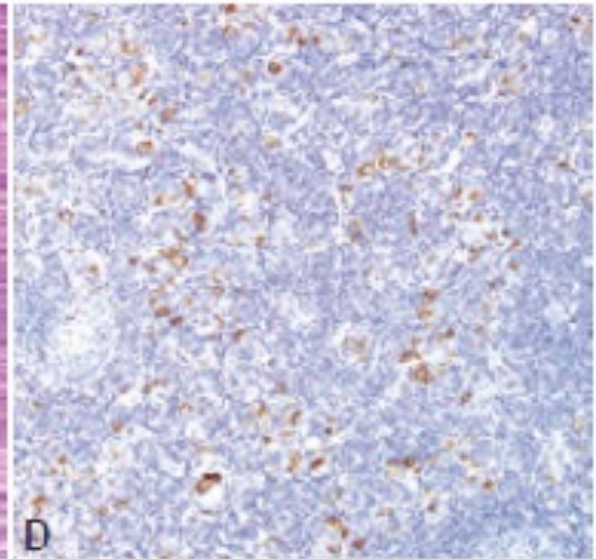
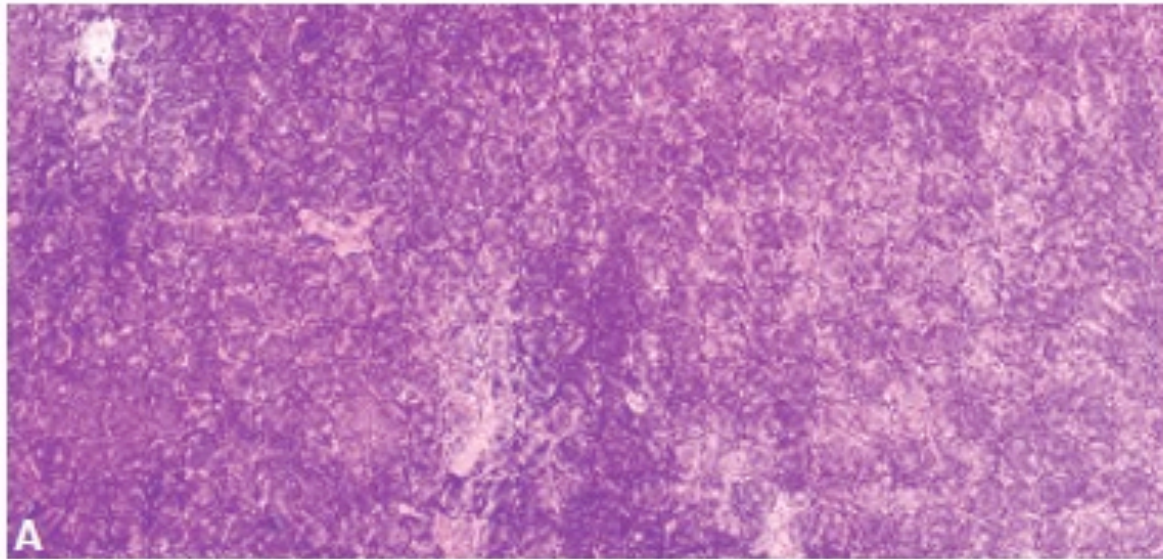


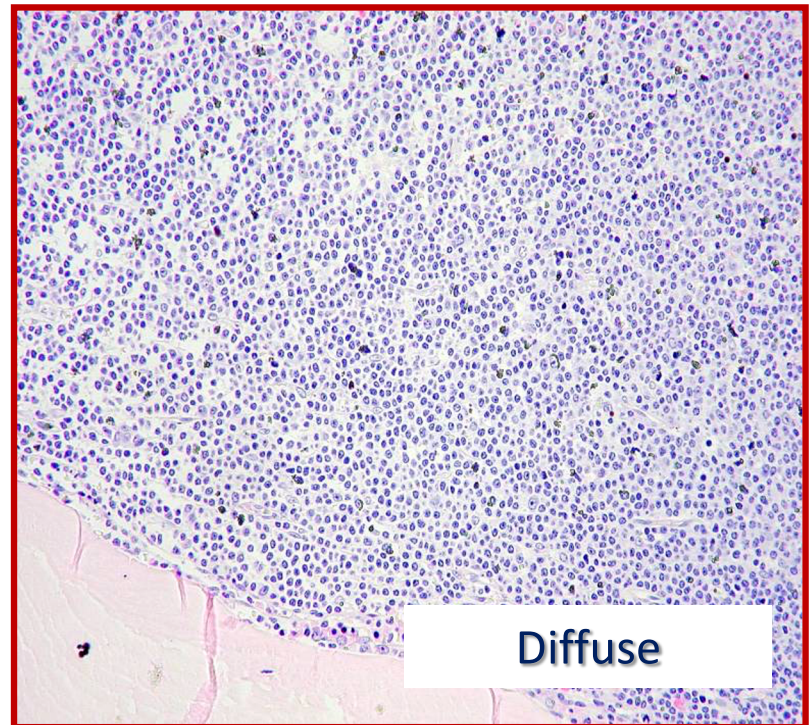
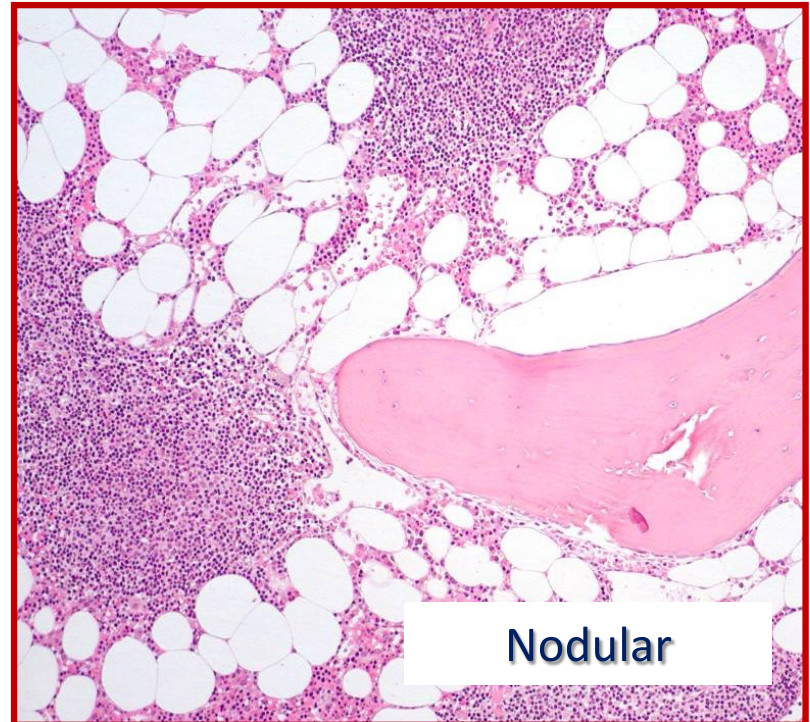
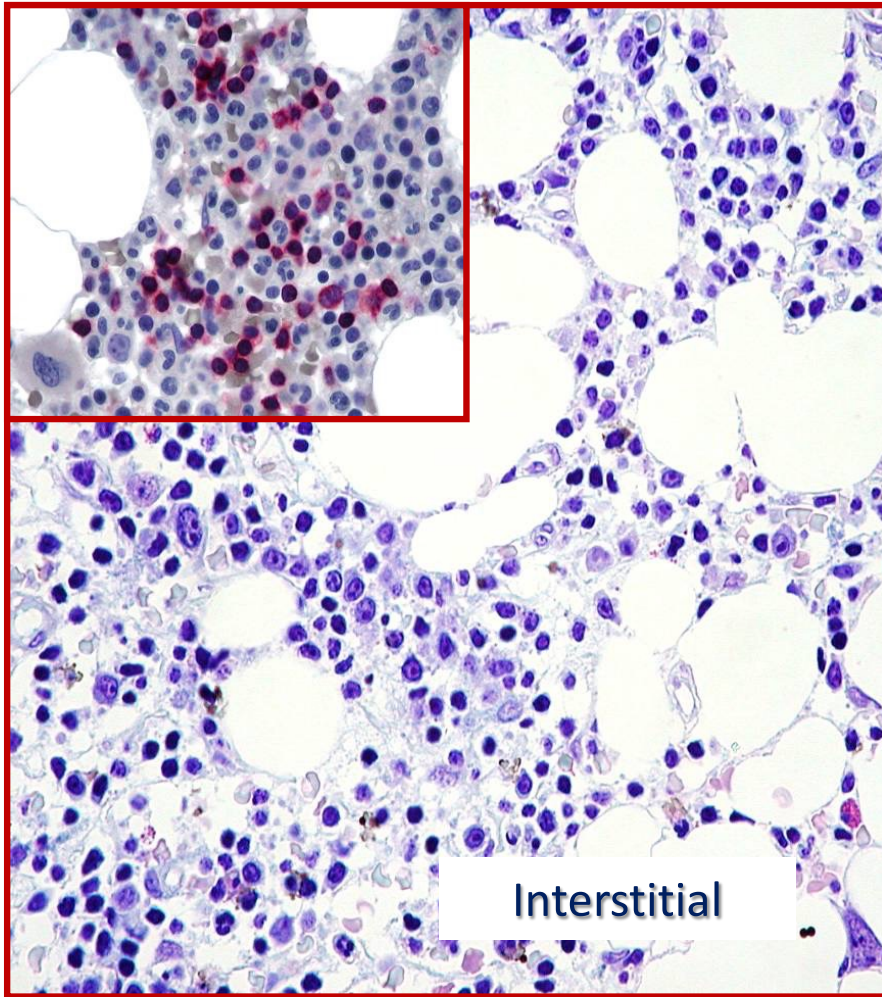
**DLBCL**

**Residual CLL**

**DLBCL**

## Richter Syndrome – Hodgkin type





Bone-marrow involvement

Pseudo-follicles (clear centres)

Useful for the diagnosis

# Phenotype

CD20 + (weak but stronger in pseudo-follicles)

CD19, CD22, CD79a (homogeneously strong)

CD5 + (variable but stronger in pseudo-follicles)

CD23 + (variable but stronger in pseudo-follicles)

IgM/IgD+ (weak)

CD200 +

LEF1 +

ZAP70 (related to the IGVH mutational status: 85% concordance)

IRF4 (+ in pseudo-follicles)

Cyclin D1 - (rare cases with weak, partial staining in the absence of t(11;14) and SOX11 positivity)

IRTA1, MNDA, T-bet -

CD10, BCL6, LMO2 -

Ki-67 + (higher in pseudo-follicles)

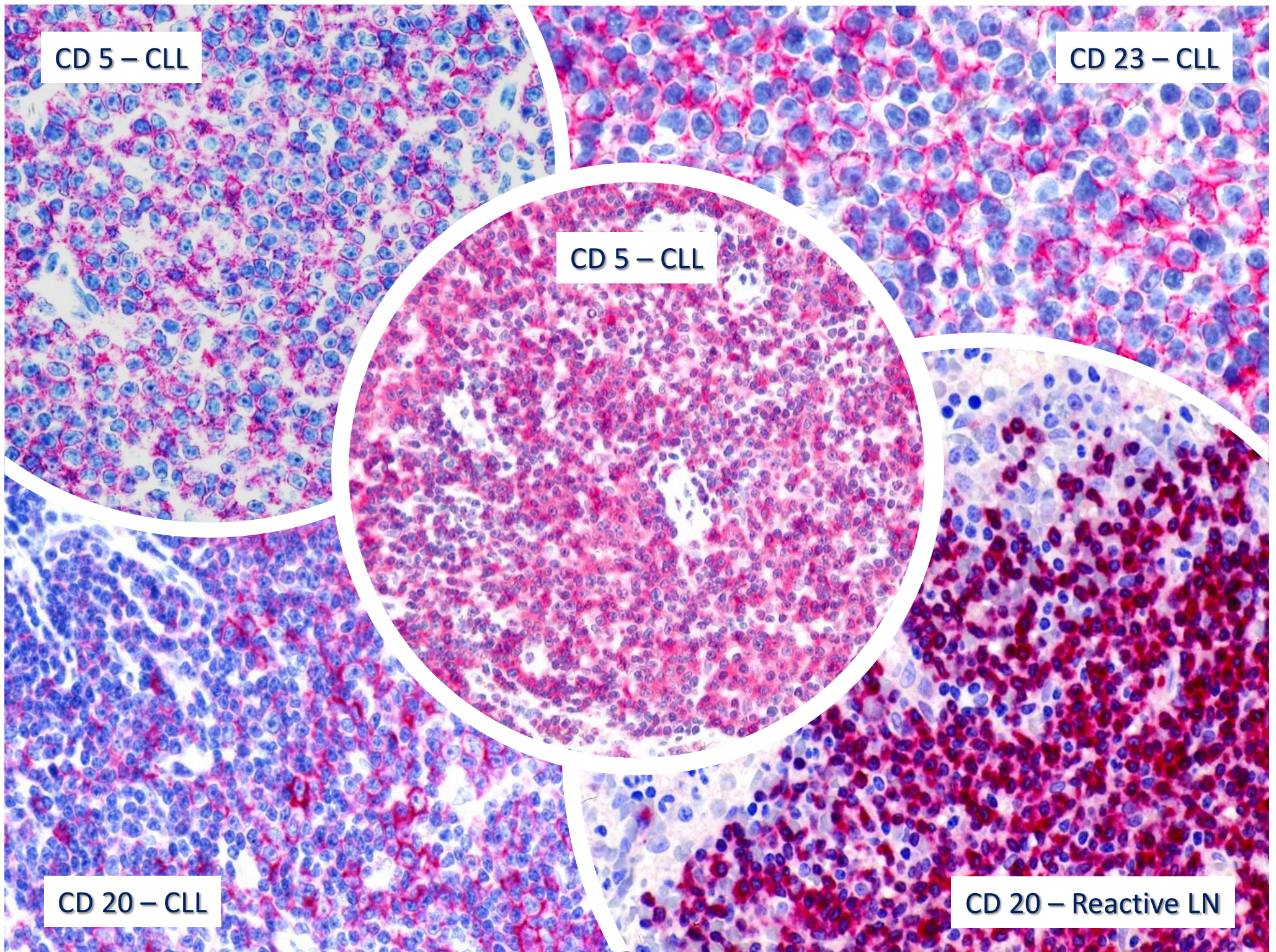
CD 5 – CLL

CD 23 – CLL

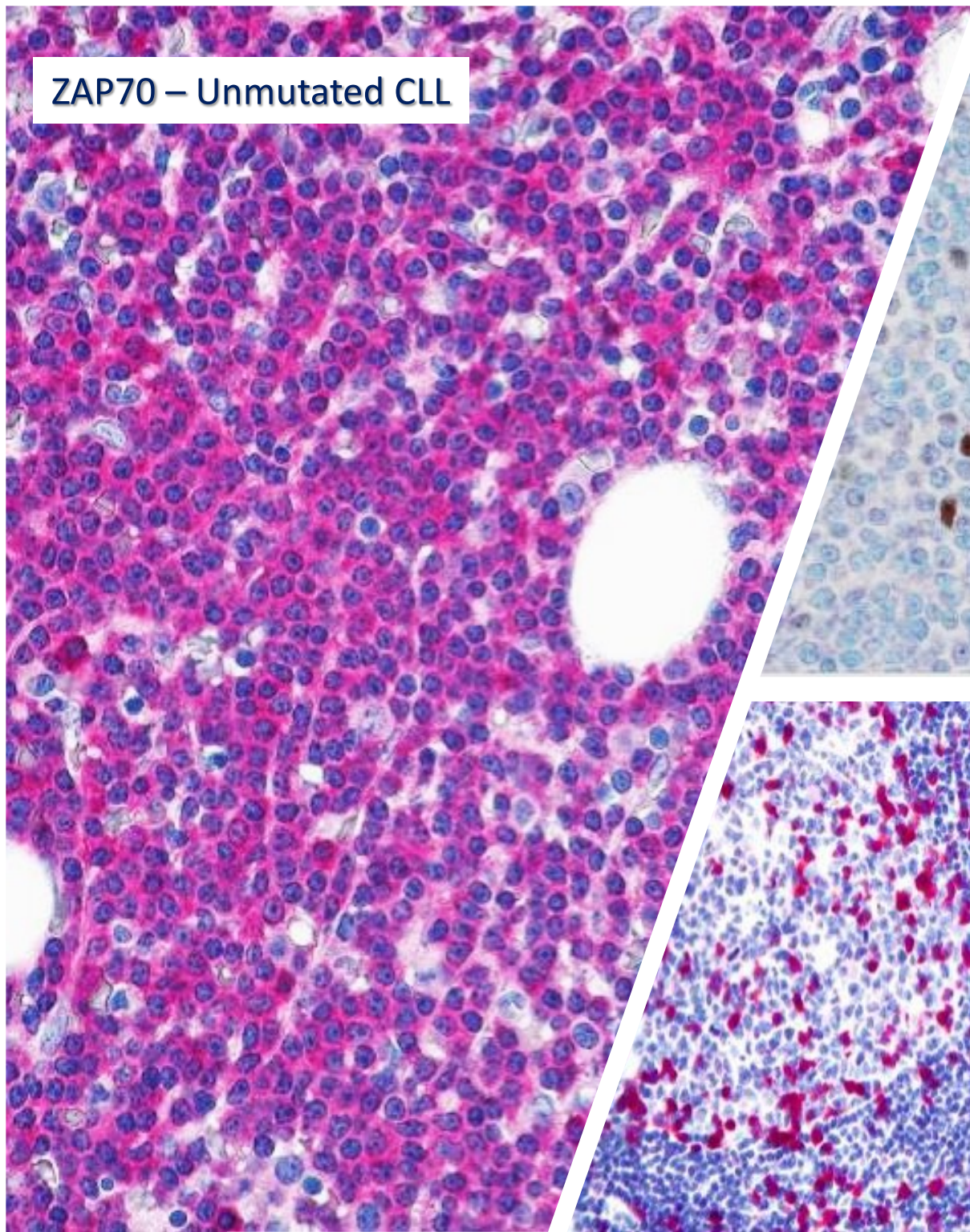
CD 5 – CLL

CD 20 – CLL

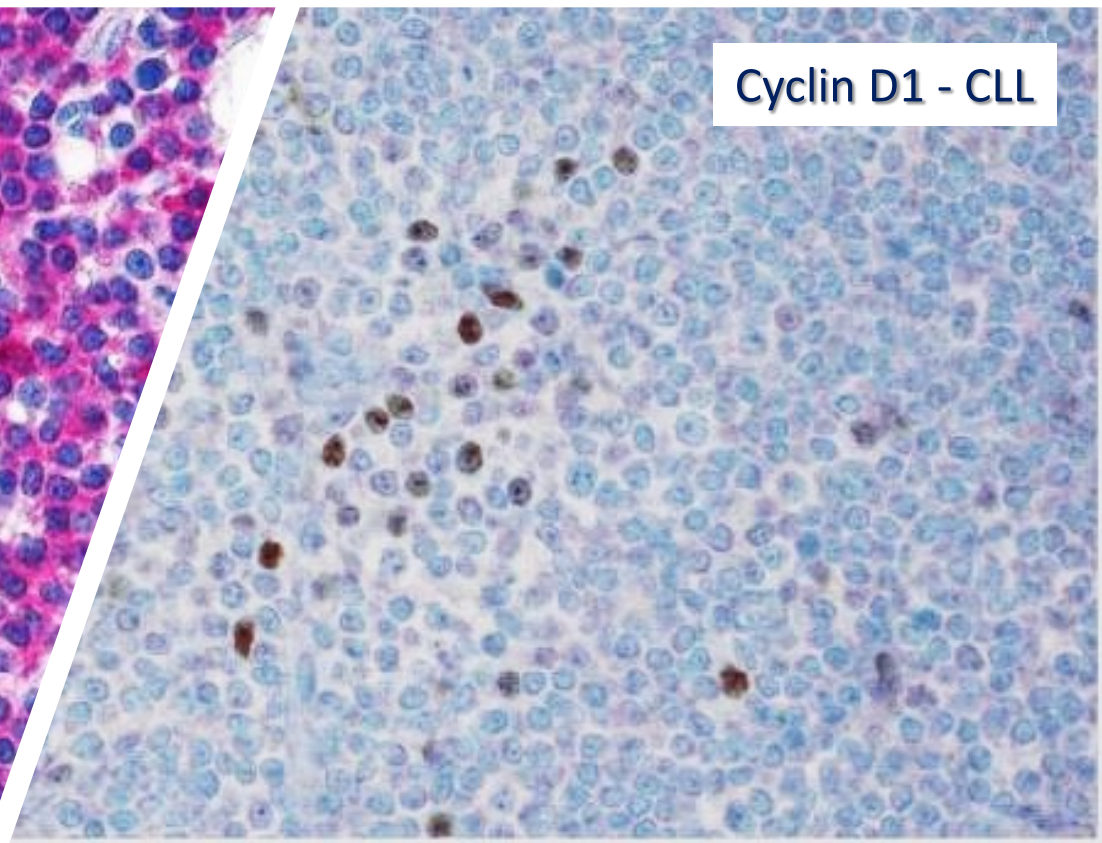
CD 20 – Reactive LN



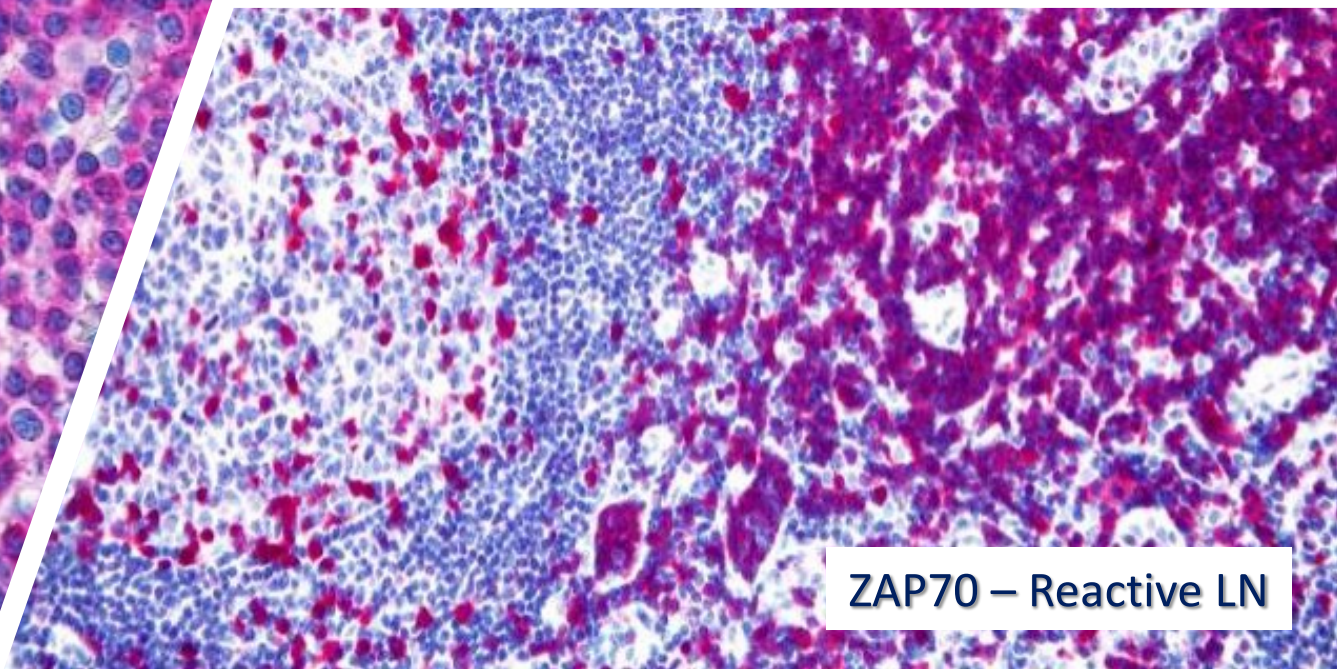
ZAP70 – Unmutated CLL



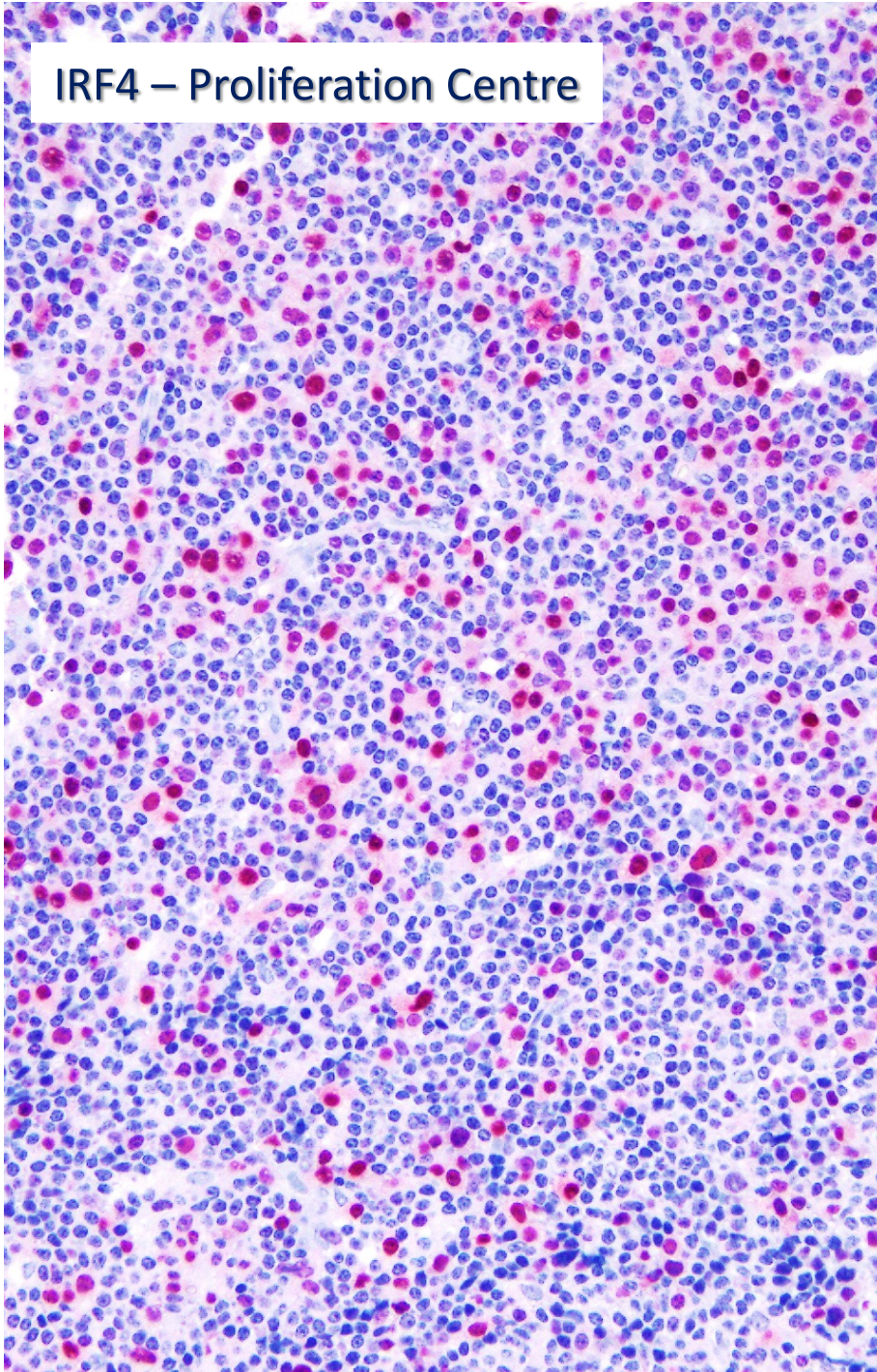
Cyclin D1 - CLL



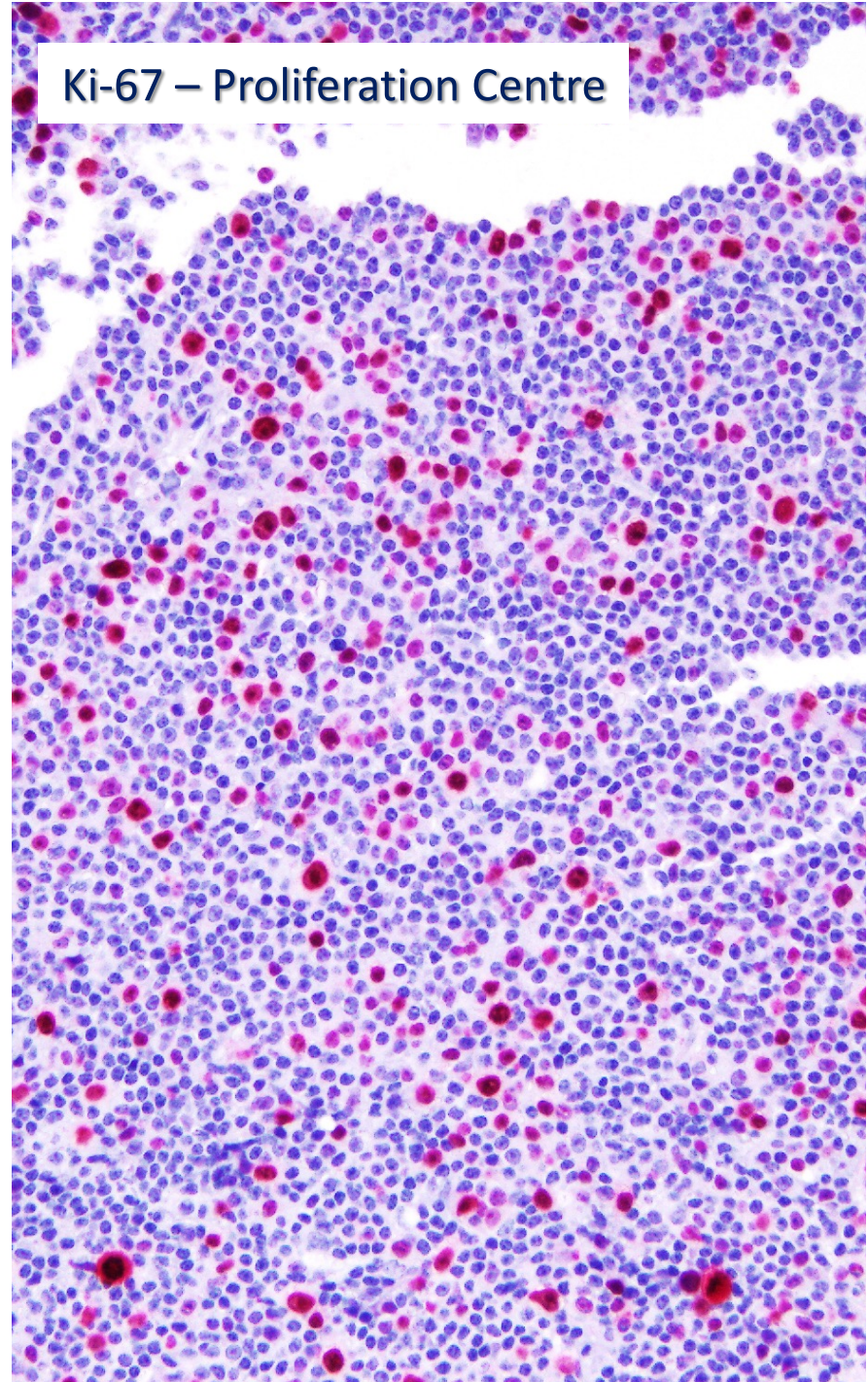
ZAP70 – Reactive LN



IRF4 – Proliferation Centre



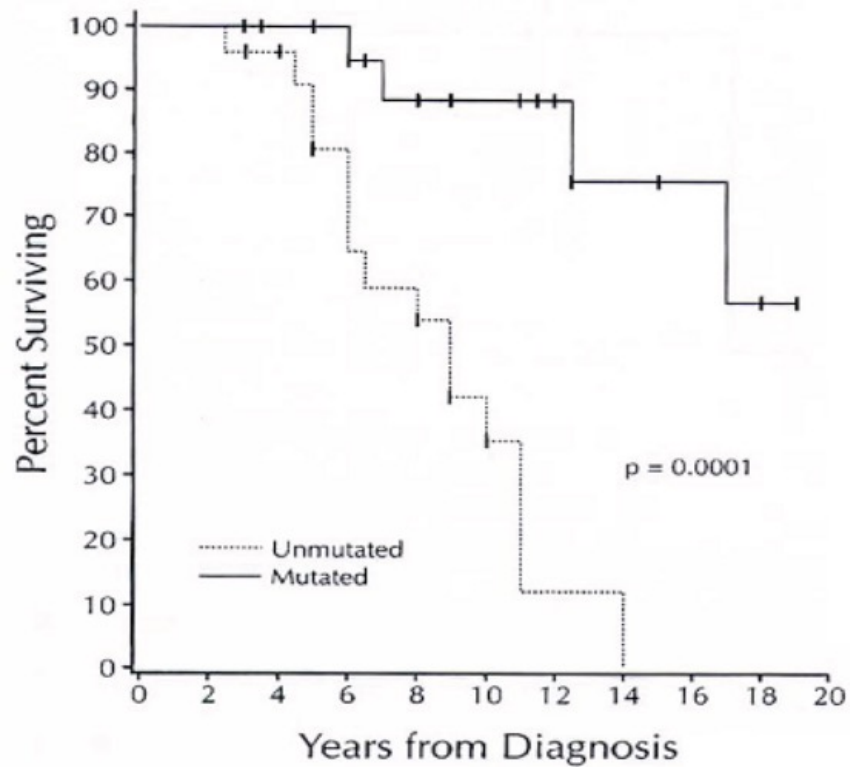
Ki-67 – Proliferation Centre



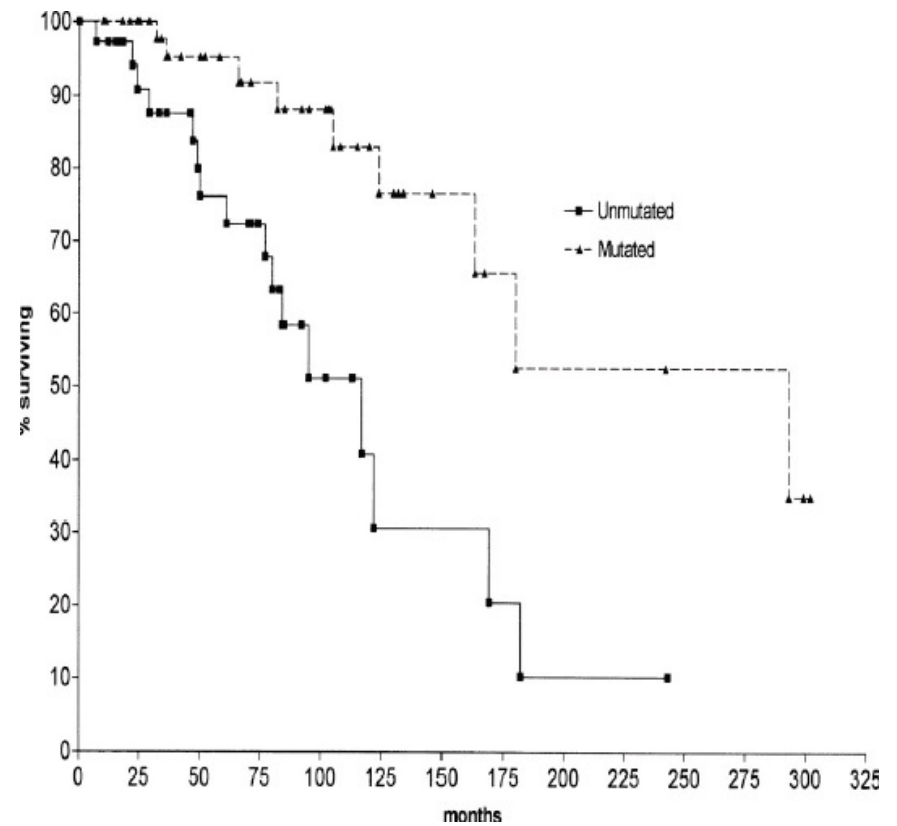


# Molecular diagnostics

- BCR (IGHV) sequencing:
- Mutated (<98% identity with the germline configuration) (50 -70 %)
- Unmutated (>98% identity with the germline configuration) (30 -50%).
- Stereotyped subsets
- Cytogenetics/FISH
- Sequencing/NGS



Damle et al Blood 1999



Hamblin et al Blood 1999

Result summary: W299	Productive IGH rearranged sequence (no stop codon and in-frame junction)		
V-GENE and allele	<a href="#">Homsap IGHV3-72*01 F</a>	score = 1299	identity = <b>93.54%</b> (275/294 nt)
J-GENE and allele	<a href="#">Homsap IGHJ3*01 F</a>	score = 205	identity = 90.00% (45/50 nt)
D-GENE and allele by IMGT/JunctionAnalysis	<a href="#">Homsap IGHD2-2*01 F</a>	D-REGION is in reading frame 2	
FR-IMGT lengths, CDR-IMGT lengths and AA JUNCTION	[25.17.38.11]	[8.10.17]	CAKVSGCSSIGCYGLDAW
JUNCTION length (in nt) and decryption	57 nt = (10)-1{7}-6(22)-3{7}-8(11)	<a href="#">(3'V)3'{N1}5'(D)3'{N2}5'(5'I)</a>	

Result summary: W86	Productive IGH rearranged sequence (no stop codon and in-frame junction)		
V-GENE and allele	<a href="#">Homsap IGHV5-10-1*03 F</a>	score = 1440	identity = <b>100.00%</b> (288/288 nt)
J-GENE and allele	<a href="#">Homsap IGHJ4*02 F</a>	score = 195	identity = 89.58% (43/48 nt)
D-GENE and allele by IMGT/JunctionAnalysis	<a href="#">Homsap IGHD6-19*01 F</a>	D-REGION is in reading frame 3	
FR-IMGT lengths, CDR-IMGT lengths and AA JUNCTION	[25.17.38.11]	[8.8.14]	CAREQWLGPNSPFDYW
JUNCTION length (in nt) and decryption	48 nt = (9)0{3}-8(13)0{11}-5(12)	<a href="#">(3'V)3'{N1}5'(D)3'{N2}5'(5'I)</a>	

#### KEY POINTS

- In a series of 29 856 CLL patients, the incidence of BcR stereotypy peaked at 41%.
- Higher-order relations exist between stereotyped subsets, particularly for those from U-CLL, for which satellite subsets were identified.

Chronic lymphocytic leukemia (CLL) is characterized by the existence of subsets of patients with (quasi)identical, stereotyped B-cell receptor (BcR) immunoglobulins. Patients in certain major stereotyped subsets often display remarkably consistent clinicobiological profiles, suggesting that the study of BcR immunoglobulin stereotypy in CLL has important implications for understanding disease pathophysiology and refining clinical decision-making. Nevertheless, several issues remain open, especially pertaining to the actual frequency of BcR immunoglobulin stereotypy and major subsets, as well as the existence of higher-order connections between individual subsets. To address these issues, we investigated clonotypic IGHV-IGHD-IGHJ gene rearrangements in a series of 29 856 patients with CLL, by far the largest series worldwide. We report that the stereotyped fraction of CLL peaks at 41% of the entire cohort and that all 19 previously identified major subsets retained their relative size and ranking, while 10 new ones emerged; overall, major stereotyped subsets had a cumulative frequency of 13.5%. Higher-level

relationships were evident between subsets, particularly for major stereotyped subsets with unmutated IGHV genes (U-CLL), for which close relations with other subsets, termed "satellites," were identified. Satellite subsets accounted for 3% of the entire cohort. These results confirm our previous notion that major subsets can be robustly identified and are consistent in relative size, hence representing distinct disease variants amenable to compartmentalized research with the potential of overcoming the pronounced heterogeneity of CLL. Furthermore, the existence of satellite subsets reveals a novel aspect of repertoire restriction with implications for refined molecular classification of CLL. (*Blood*. 2021;137(10):1365-1376)

## Cytogenetics/FISH

Aberration(s)	Frequency	
	Mutated IGHV n = 132 (44% of cases)	Unmutated IGHV n = 168 (56% of cases)
Clonal aberrations	80%	84%
13q deletion*	65%	48%
Isolated 13q deletion*	50%	26%
Trisomy 12	15%	19%
11q deletion*	4%	27%
17p deletion*	3%	10%
17p or 11q deletion*	7%	35%

\*Significant difference between cases with and without IGHV mutation.

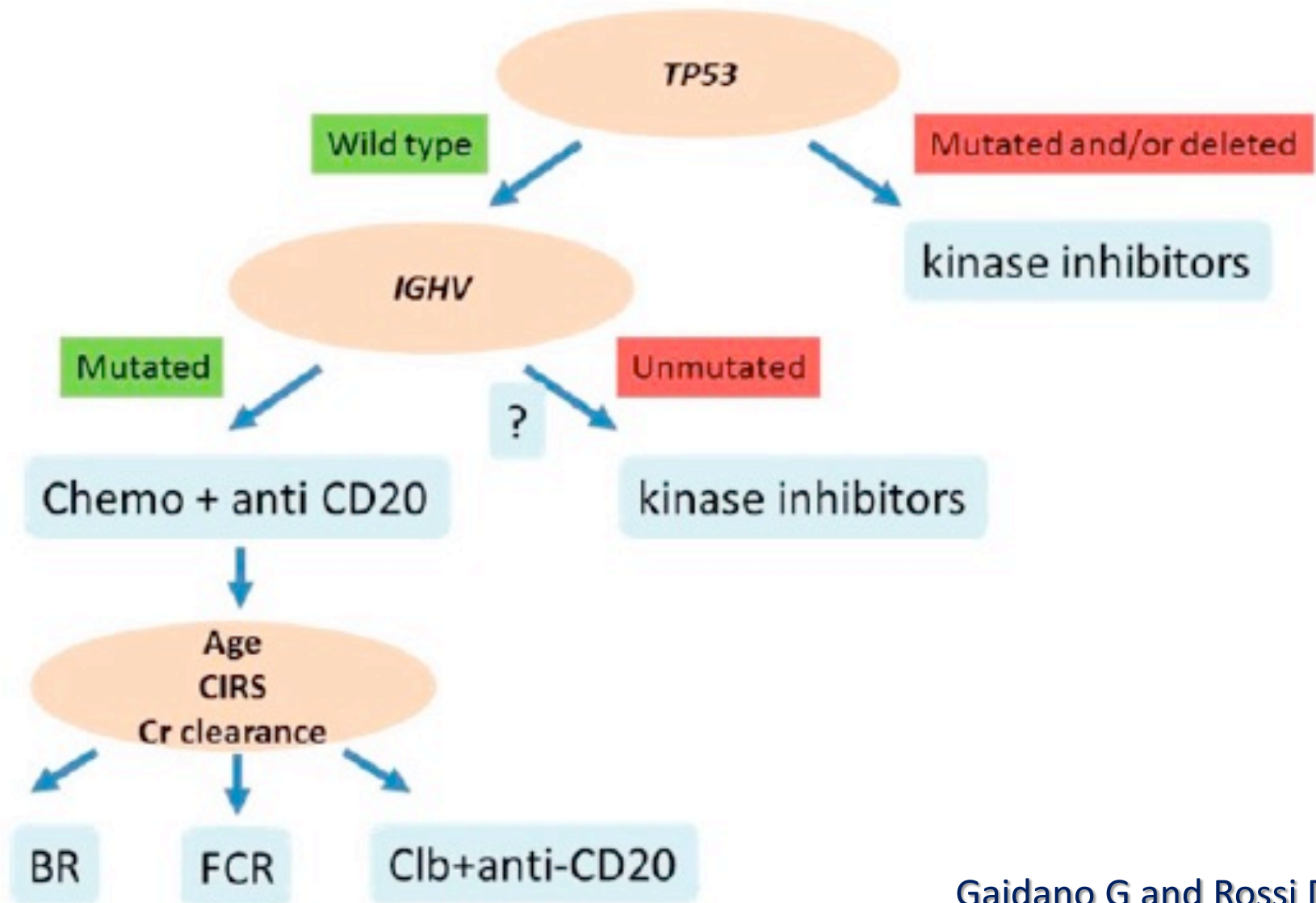


Gaidano G and Rossi D

## **Integrated mutational and cytogenetic analysis identifies new prognostic subgroups in chronic lymphocytic leukemia**

Davide Rossi,<sup>1</sup> Silvia Rasi,<sup>1</sup> Valeria Spina,<sup>1</sup> Alessio Bruscatto,<sup>1</sup> Sara Monti,<sup>1</sup> Carmela Ciardullo,<sup>1</sup> Clara Deambrogi,<sup>1</sup> Hossein Khiabani,<sup>2</sup> Roberto Serra,<sup>3</sup> Francesco Bertoni,<sup>4</sup> Francesco Forconi,<sup>5,6</sup> Luca Laurenti,<sup>7</sup> Roberto Marasca,<sup>8</sup> Michele Dal-Bo,<sup>9</sup> Francesca Maria Rossi,<sup>9</sup> Pietro Bulian,<sup>9</sup> Josep Nomdedeu,<sup>10</sup> Giovanni Del Poeta,<sup>11</sup> Valter Gattei,<sup>9</sup> Laura Pasqualucci,<sup>12-14</sup> Raul Rabadan,<sup>2</sup> \*Robin Foà,<sup>15</sup> \*Riccardo Dalla-Favera,<sup>12,13,16</sup> and \*Gianluca Gaidano<sup>1</sup>

**(*Blood*. 2013;121(8):1403-1412)**



Gaidano G and Rossi D



## **Lymphoplasmacytic lymphoma**

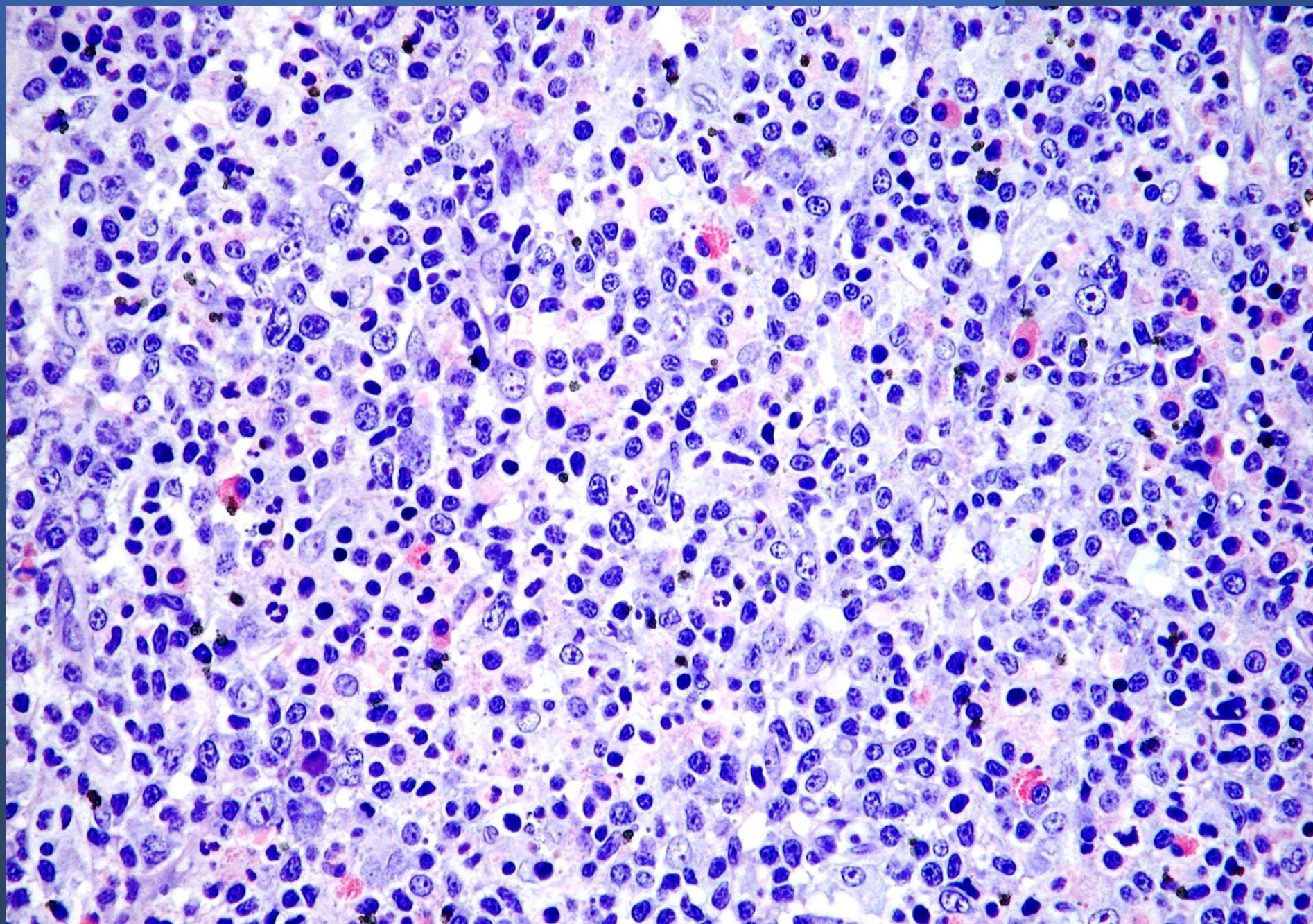
Small lymphocytes + plasmacytoid elements + plasma cells

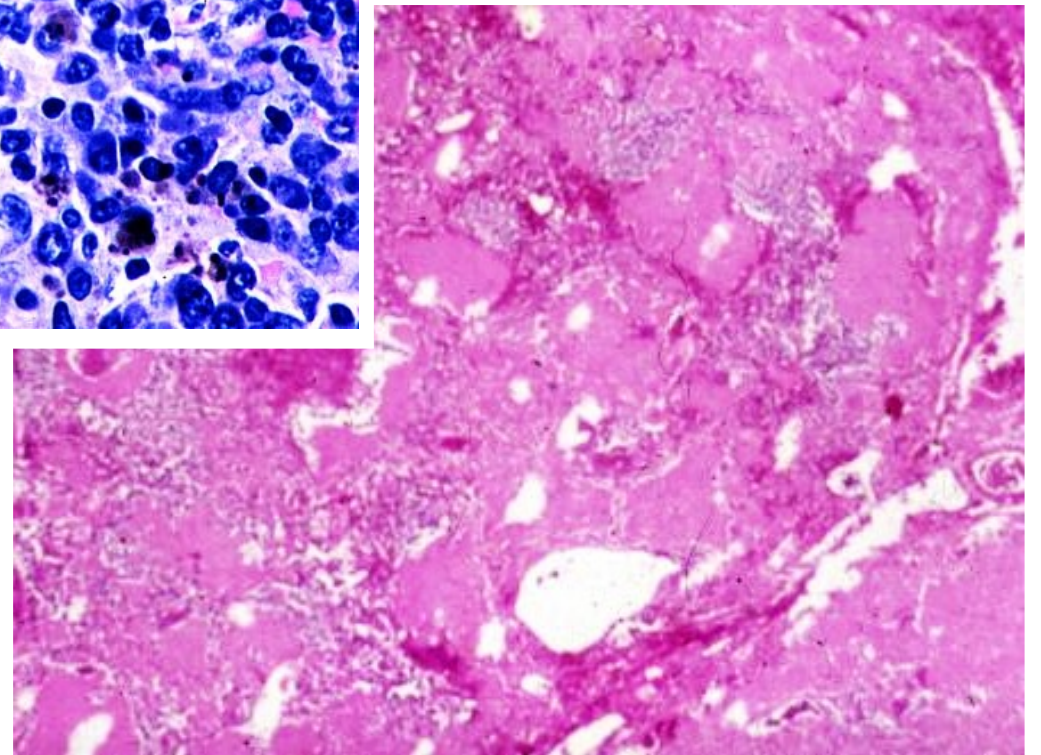
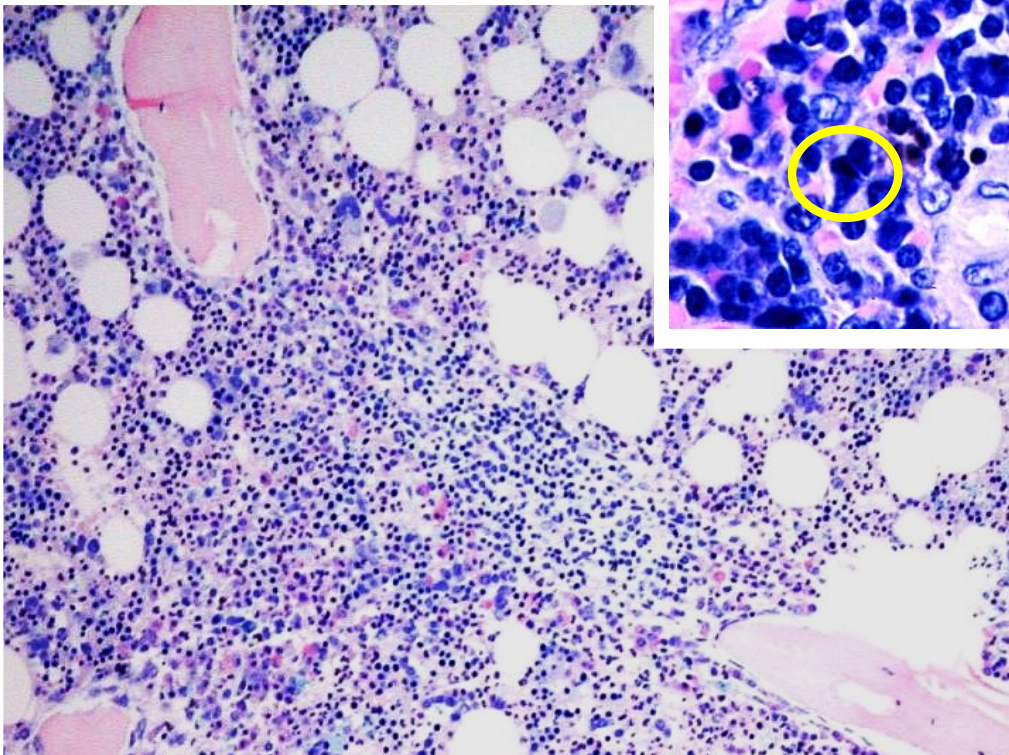
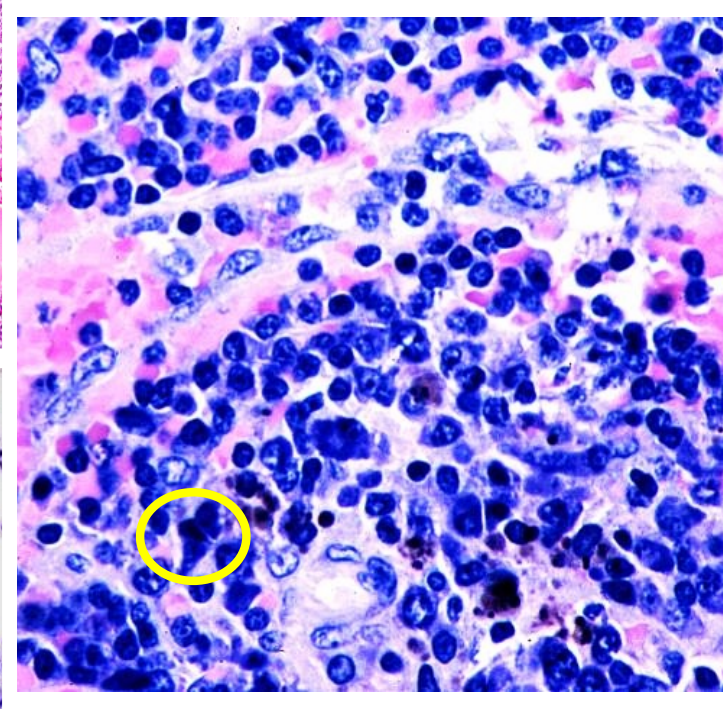
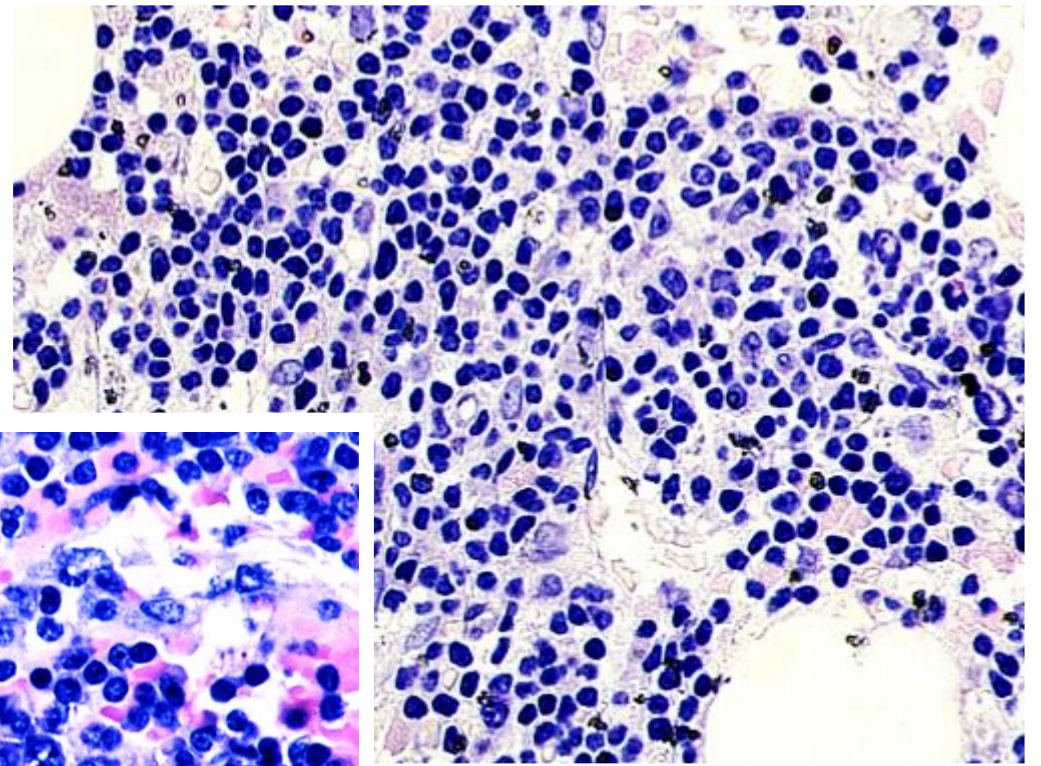
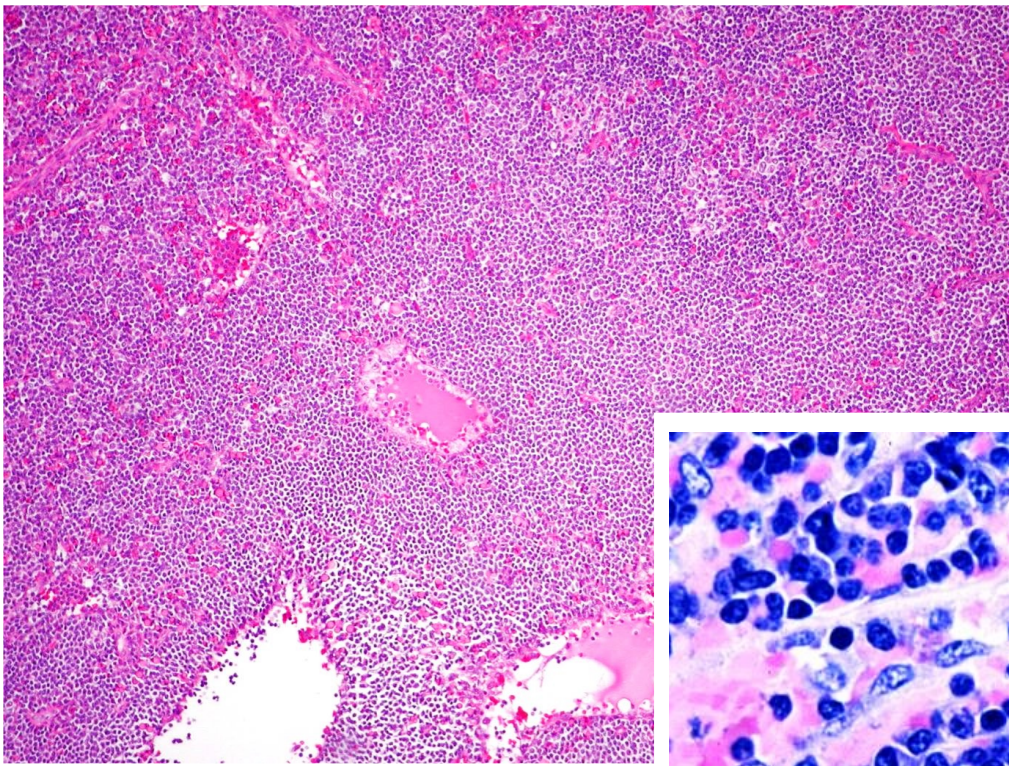
Exclusion diagnosis as other lymphomas can show plasmacellular differentiation

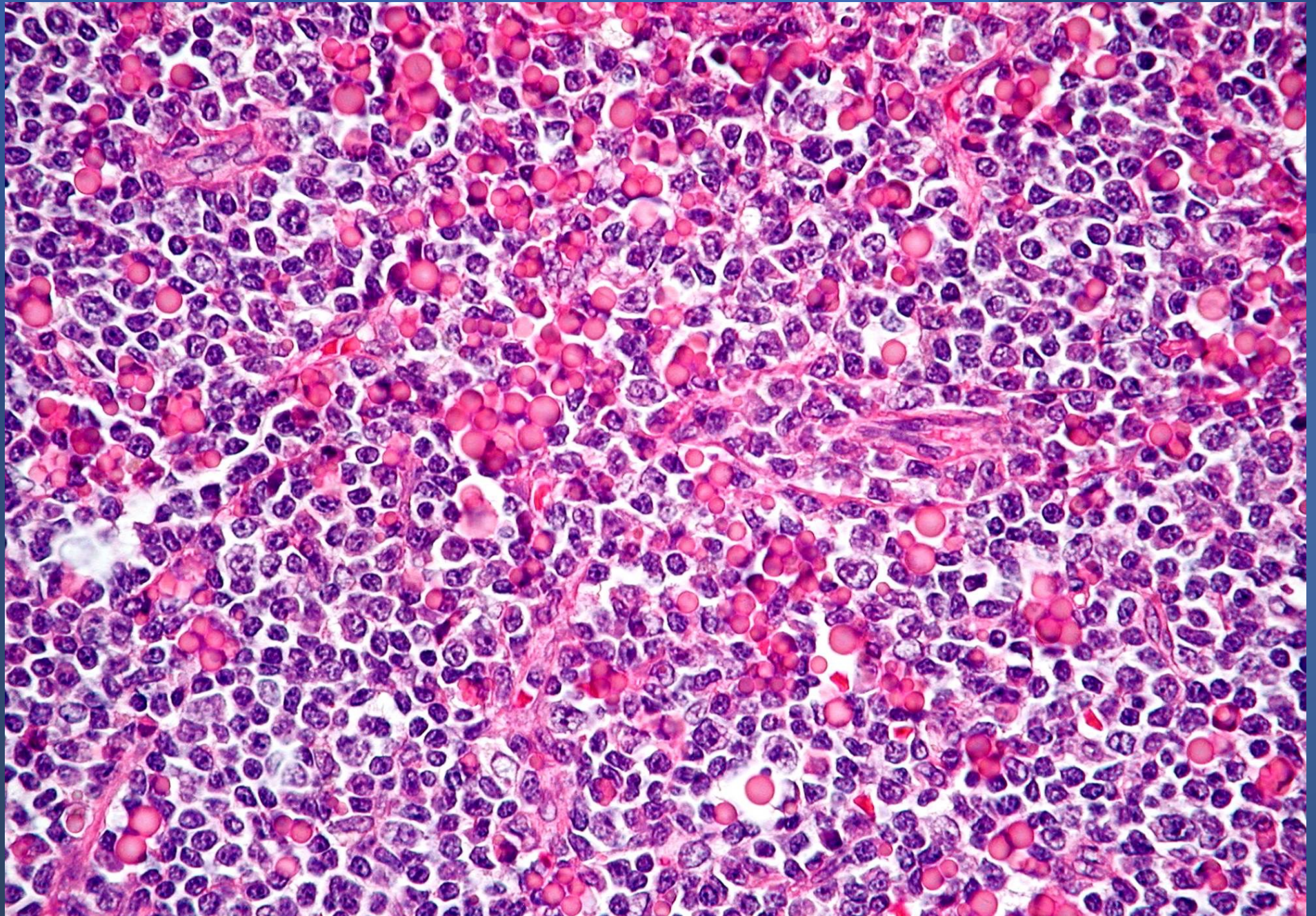
*MYD88* L265P mutation characteristic but not exclusive

IgM paraprotein not necessarily required

WM found in a substantial subset, but not synonymous of LPL







# Phenotype

CD19, CD20, CD22, CD79a, CD79b +

CD5 -

CD23 -/+

**IgM+ (CYTOPLASMIC!)**

IgD-

**CD38+**

IRF4 +/-

CD45 +/-

CD138 -

CD200 -

LEF1 -

Cyclin D1 -

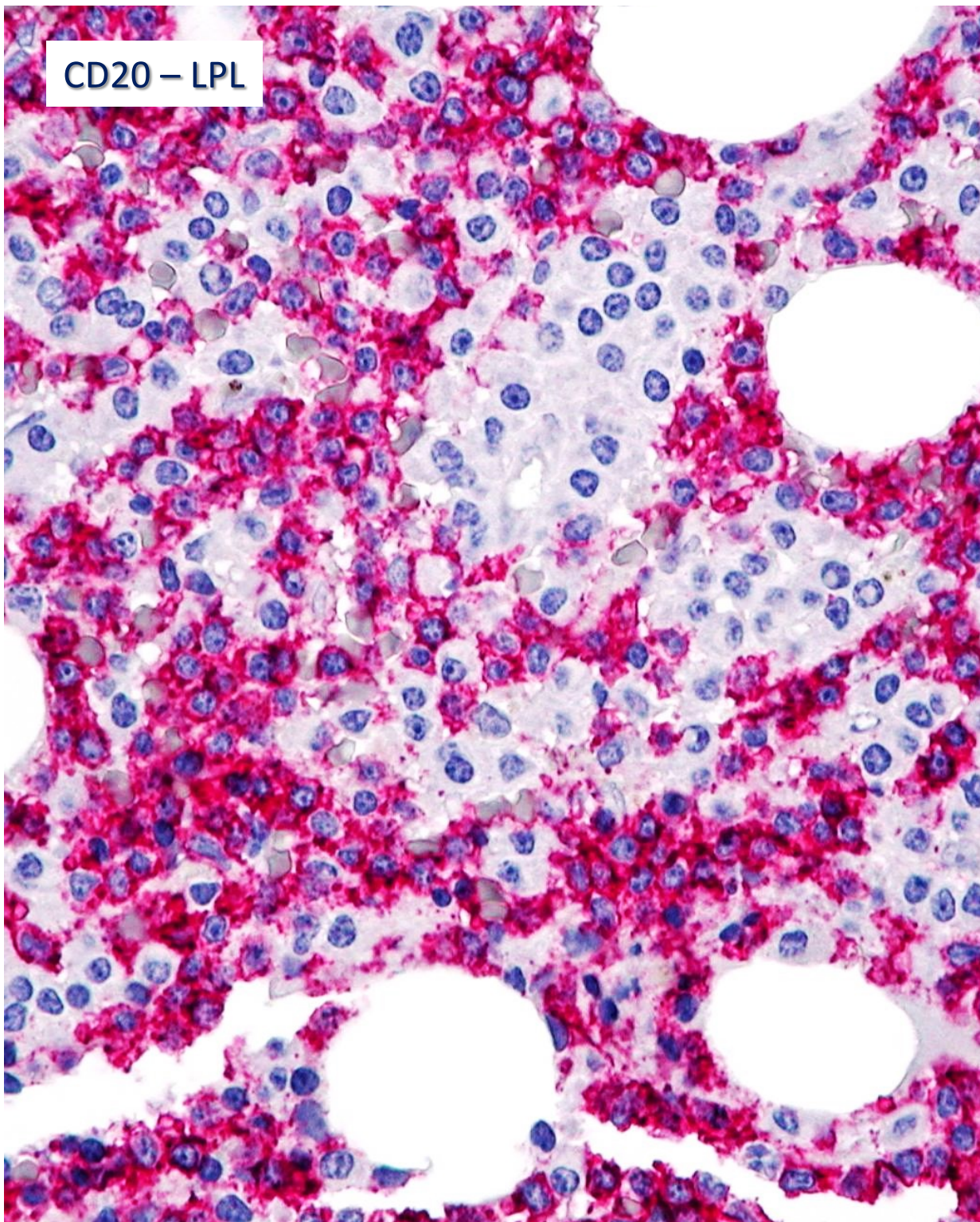
IRTA1, MNDA, T-bet -

CD10, BCL6, LMO2 -

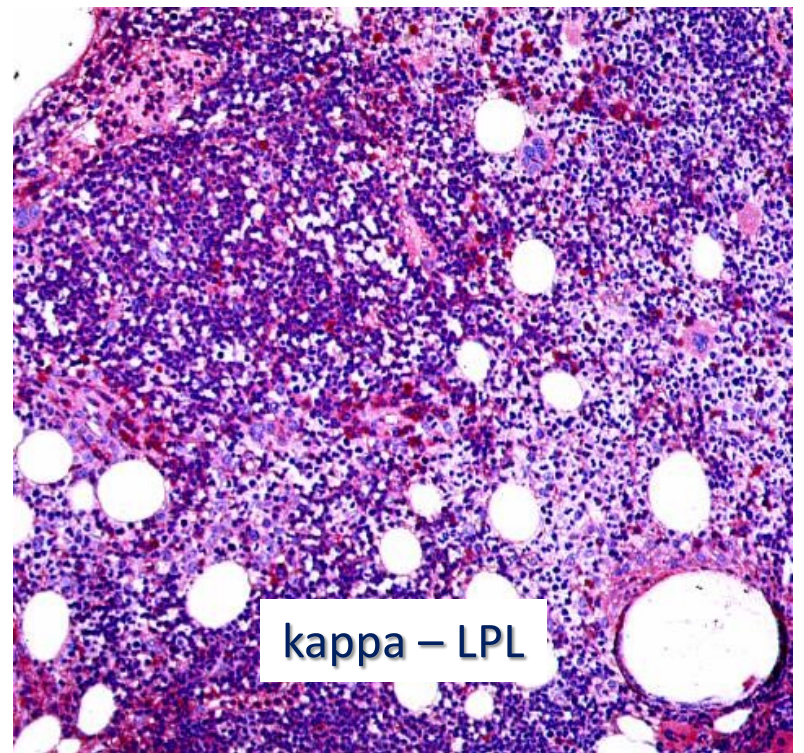
Ki-67: low



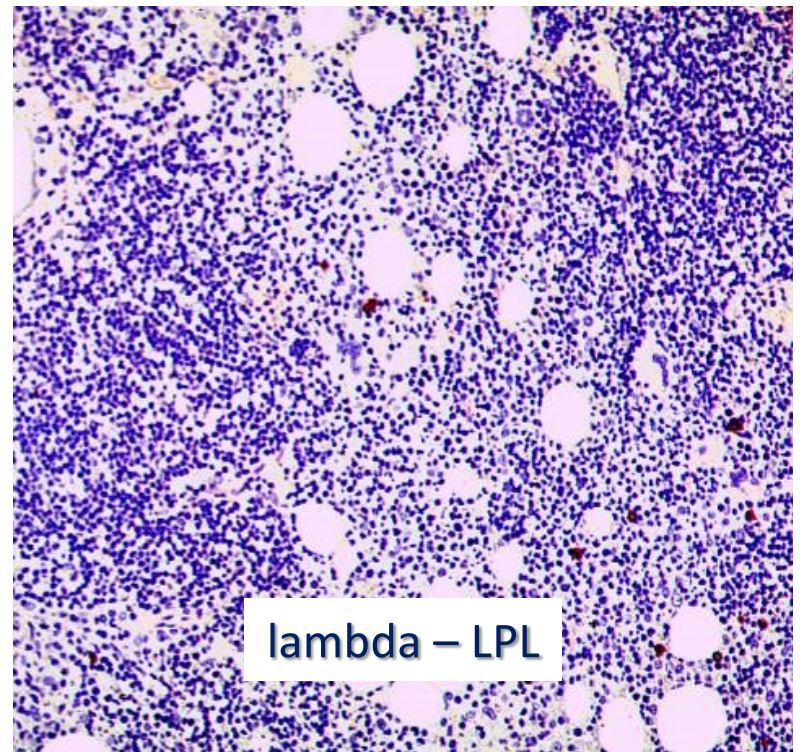
CD20 – LPL



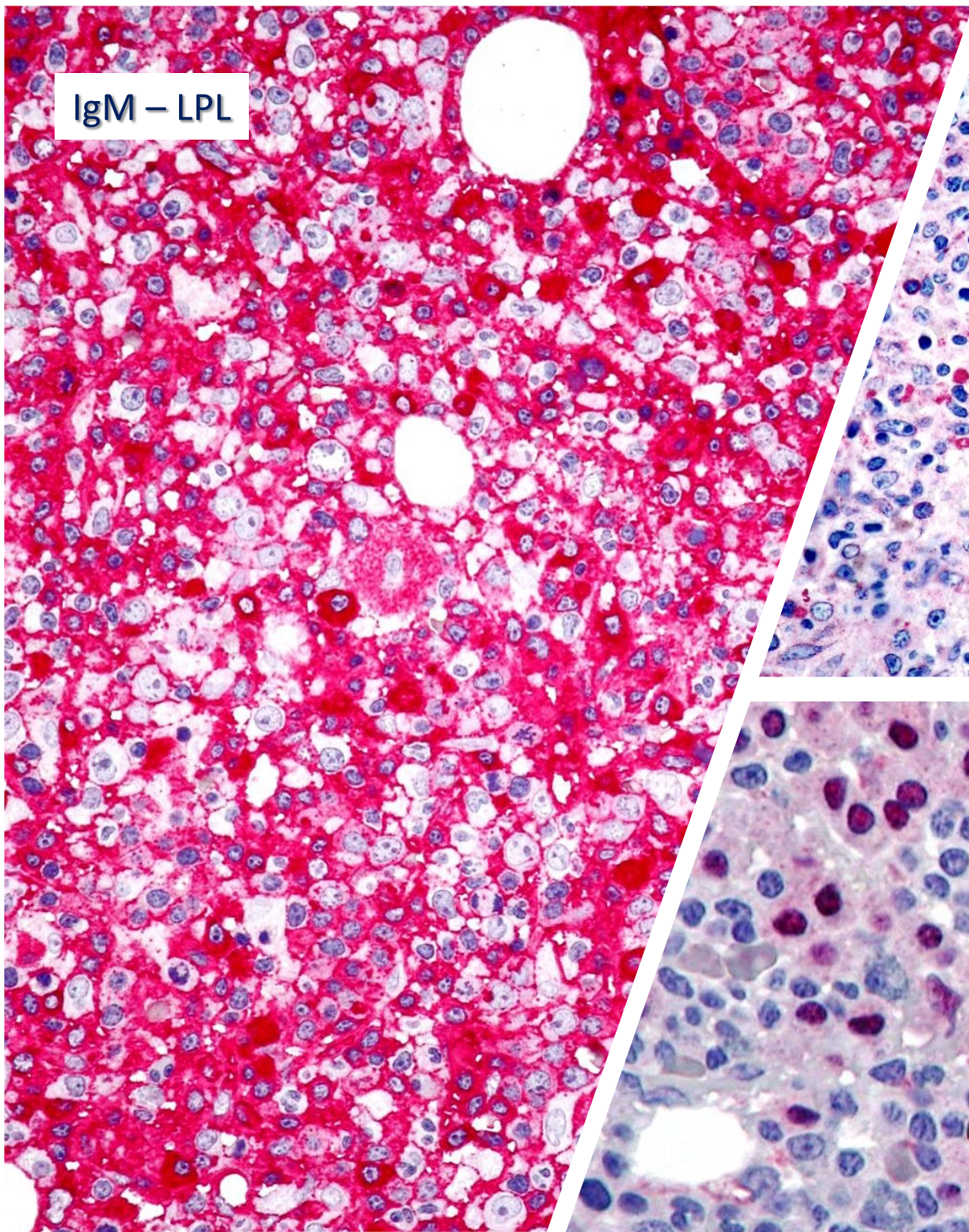
kappa – LPL



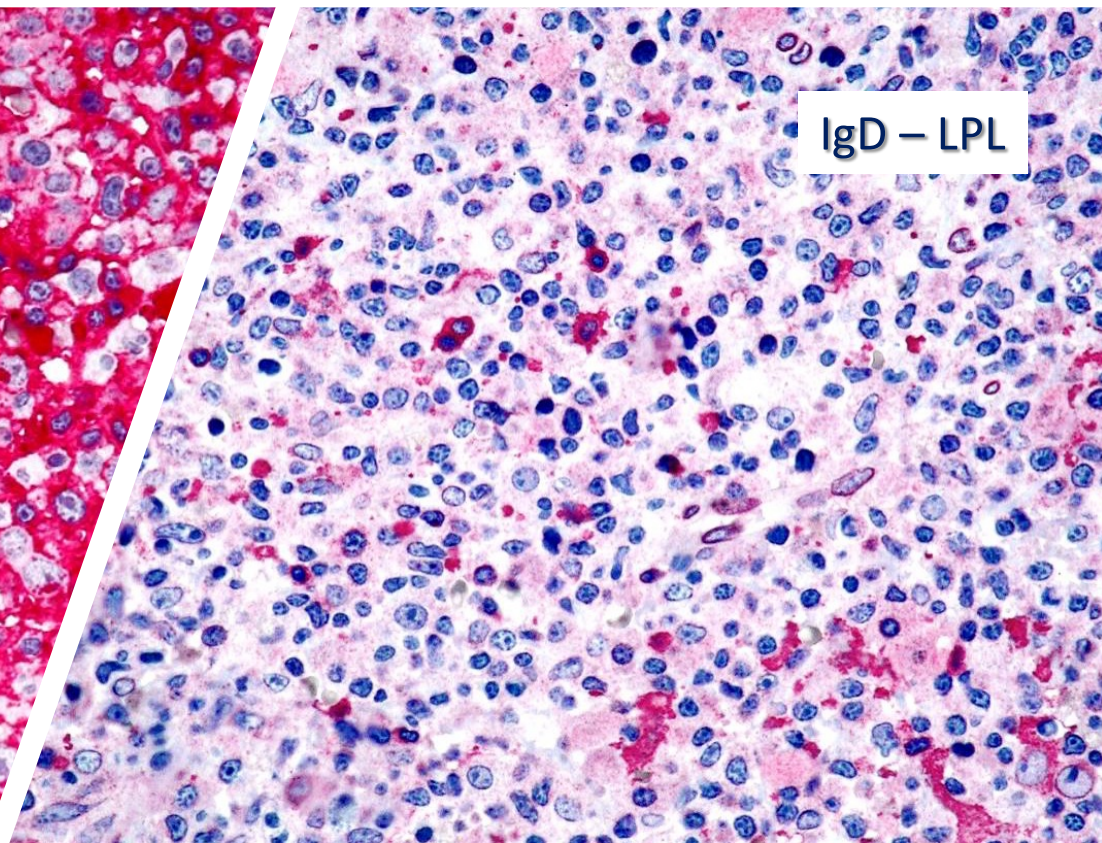
lambda – LPL



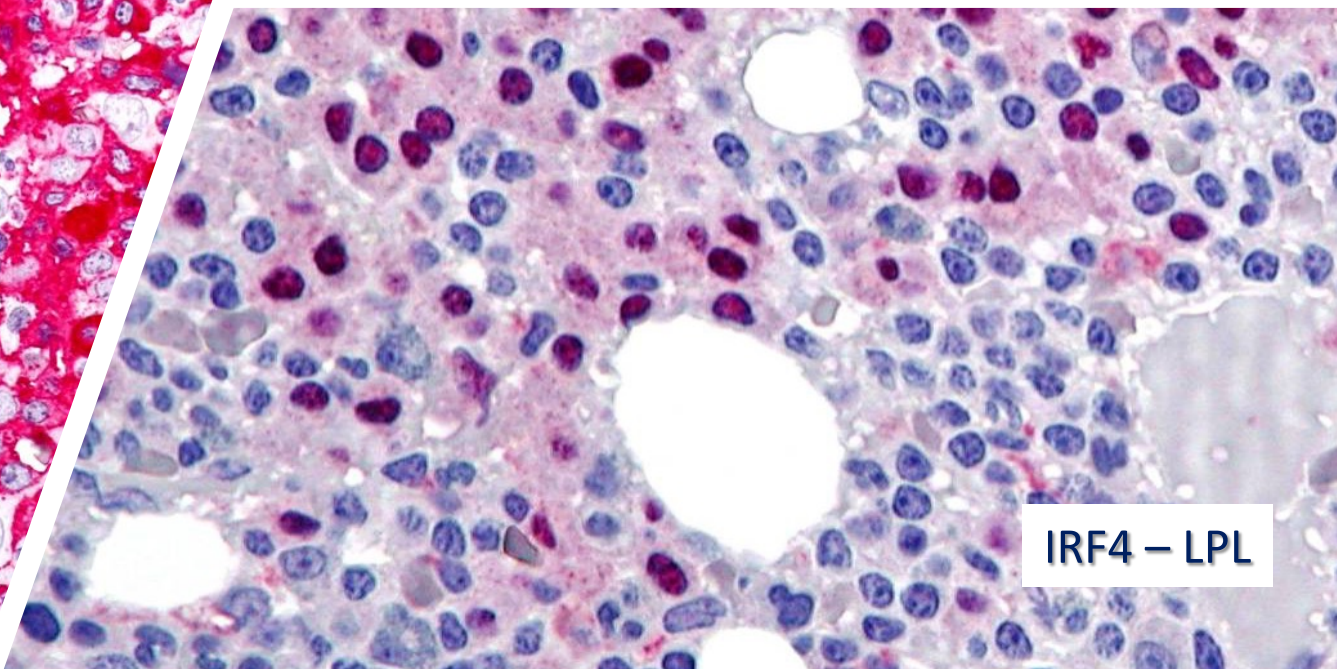
IgM - LPL



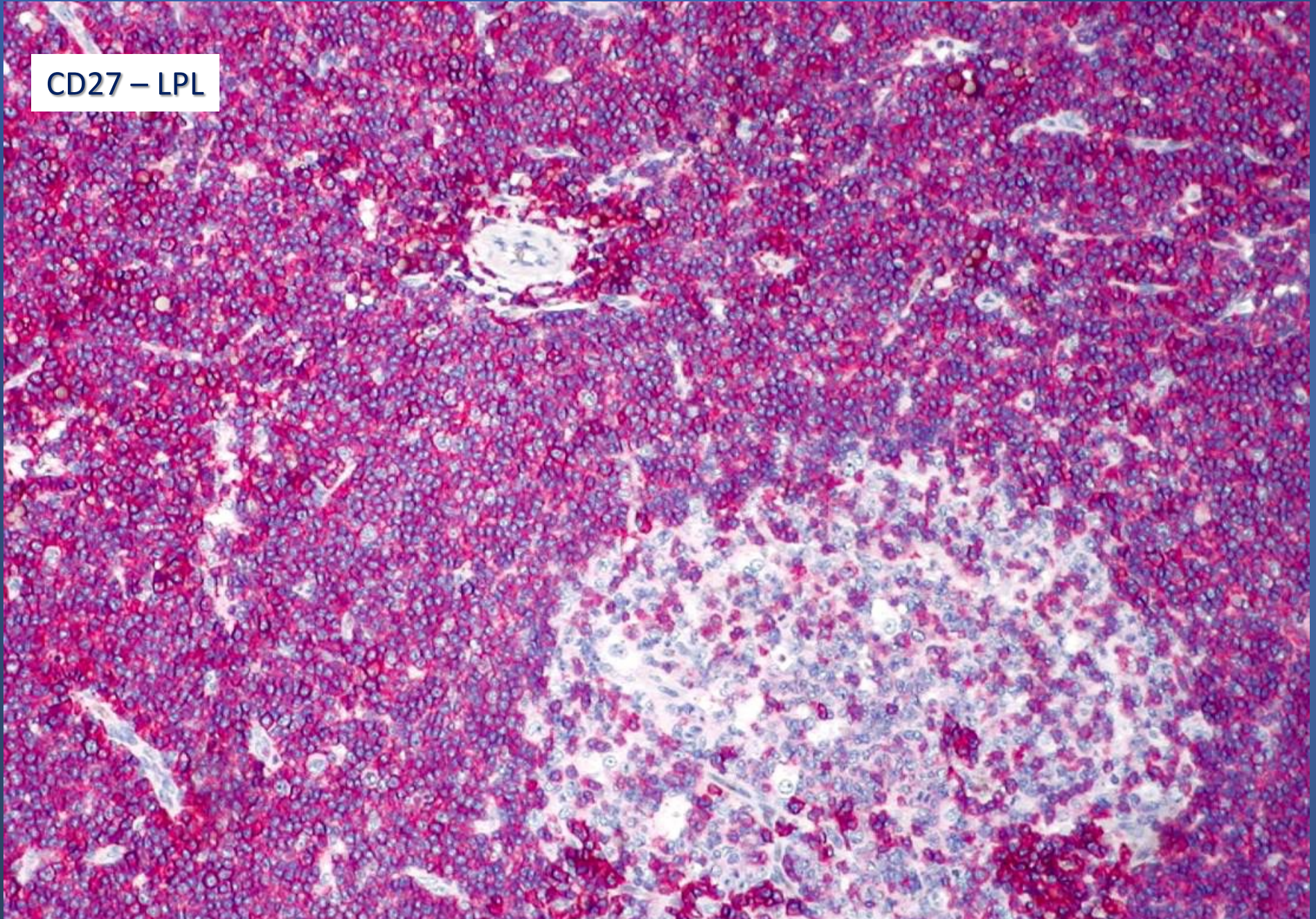
IgD - LPL



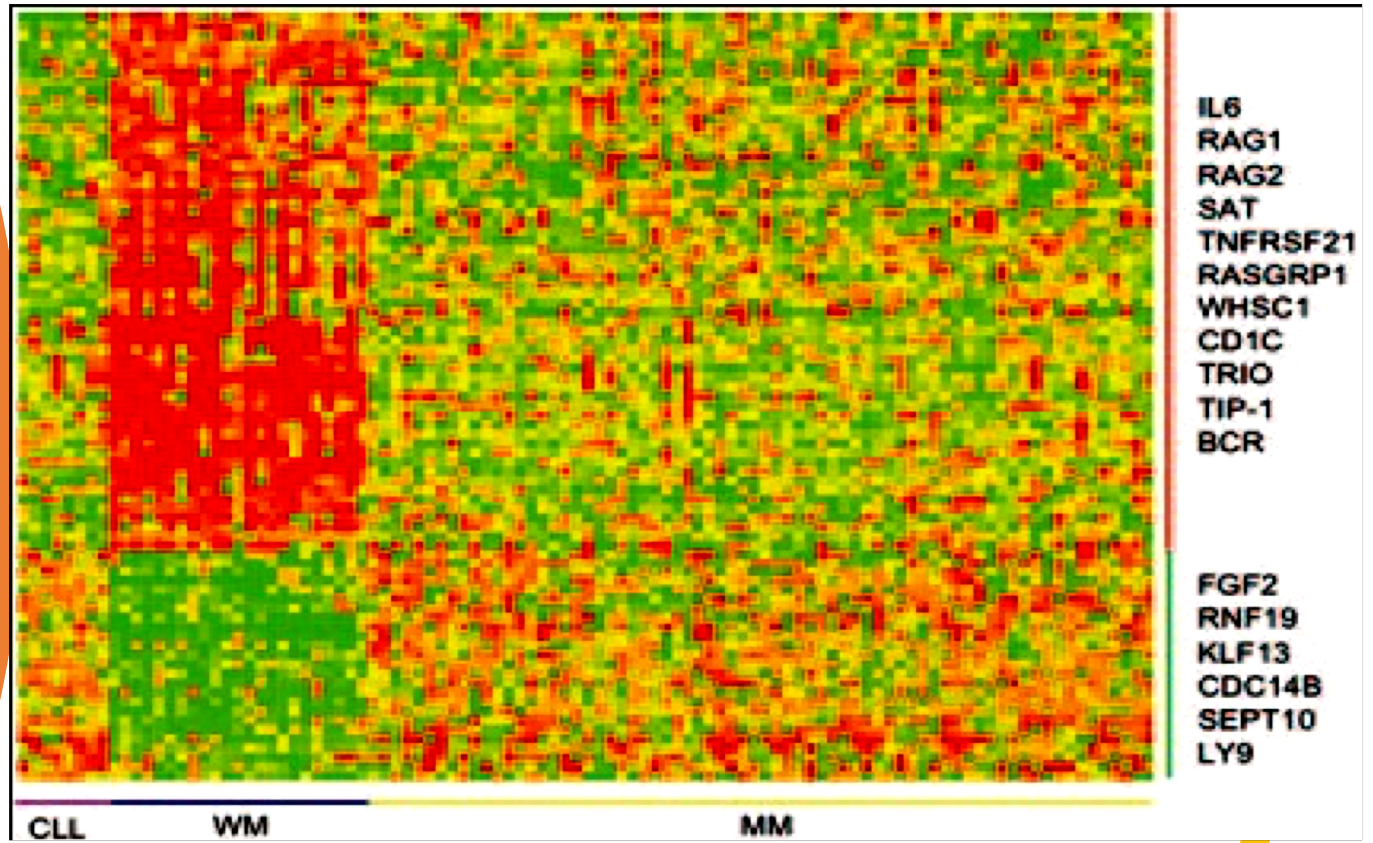
IRF4 - LPL



CD27 – LPL





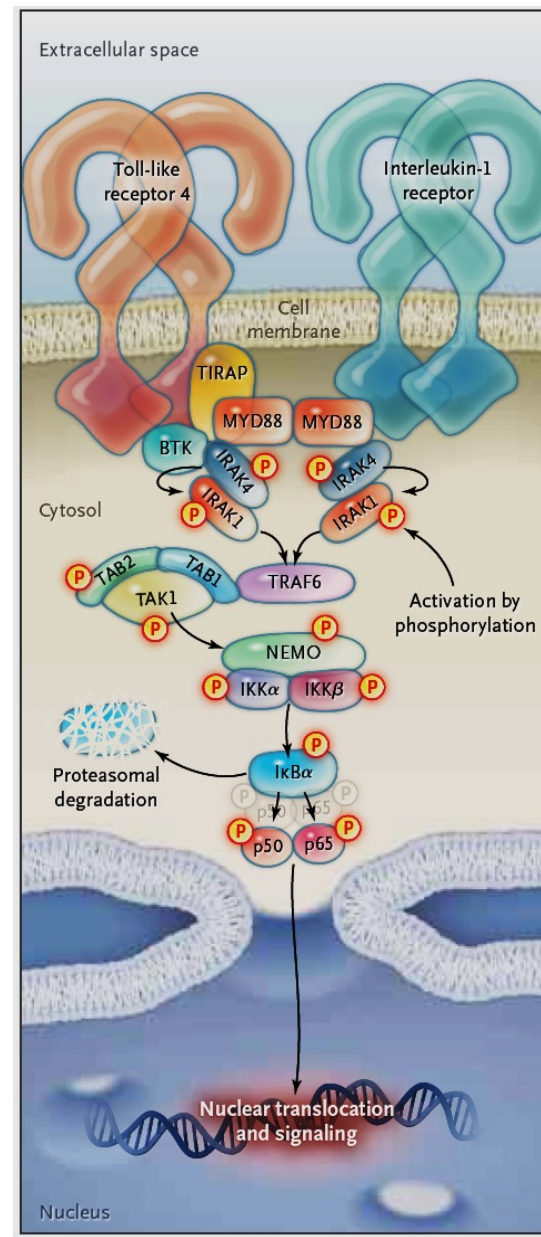


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## MYD88 L265P Somatic Mutation in Waldenström's Macroglobulinemia

Steven P. Treon, M.D., Ph.D., Lian Xu, M.S., Guang Yang, Ph.D.,  
Yangsheng Zhou, M.D., Ph.D., Xia Liu, M.D., Yang Cao, M.D.,  
Patricia Sheehy, N.P., Robert J. Manning, B.S., Christopher J. Patterson, M.A.,  
Christina Tripsas, M.A., Luca Arcaini, M.D., Geraldine S. Pinkus, M.D.,  
Scott J. Rodig, M.D., Ph.D., Aliyah R. Sohani, M.D., Nancy Lee Harris, M.D.,  
Jason M. Laramie, Ph.D., Donald A. Skifter, Ph.D., Stephen E. Lincoln, Ph.D.,  
and Zachary R. Hunter, M.A.

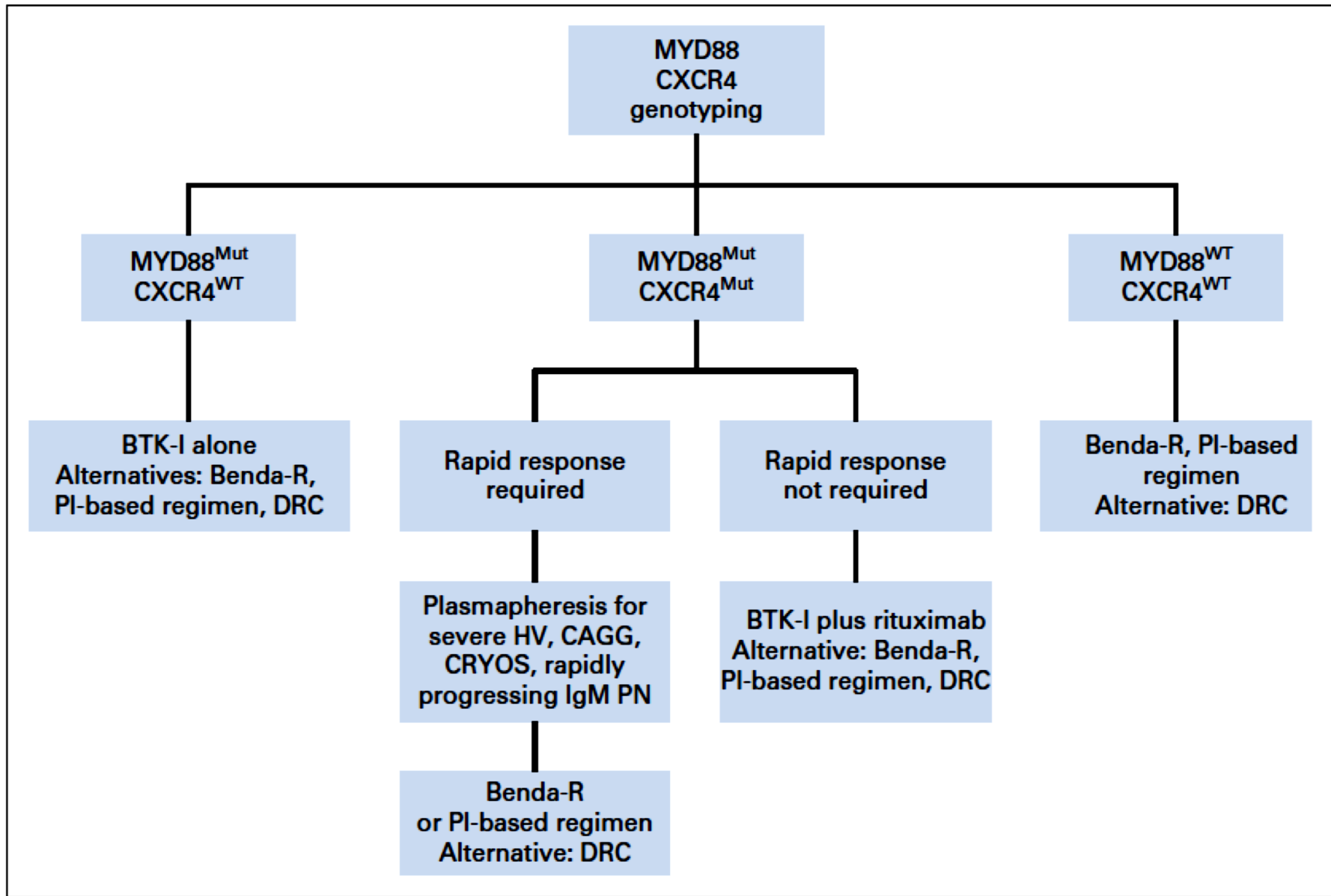


# Lymphoplasmacytic Lymphoma and Nodal Marginal Zone Lymphoma

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- *MYD88* L265P can distinguish LPL (70-100%) from NMZL (0-20%)
  - Frequency in NMZL may be overstated. Re-review reveals many of the cases are LPL
- Who to test for *MYD88* L265P
  - Classic WM diagnosis, testing likely will add little
  - Small B-cell lymphoma with plasmacytic differentiation, where LPL and other small B-cell lymphomas are in the differential diagnosis should be tested
  - *CXCR4* mutation may illuminate cases negative for *MYD88*
  - Further gene mutations: *ARID1A*, *CD79B*

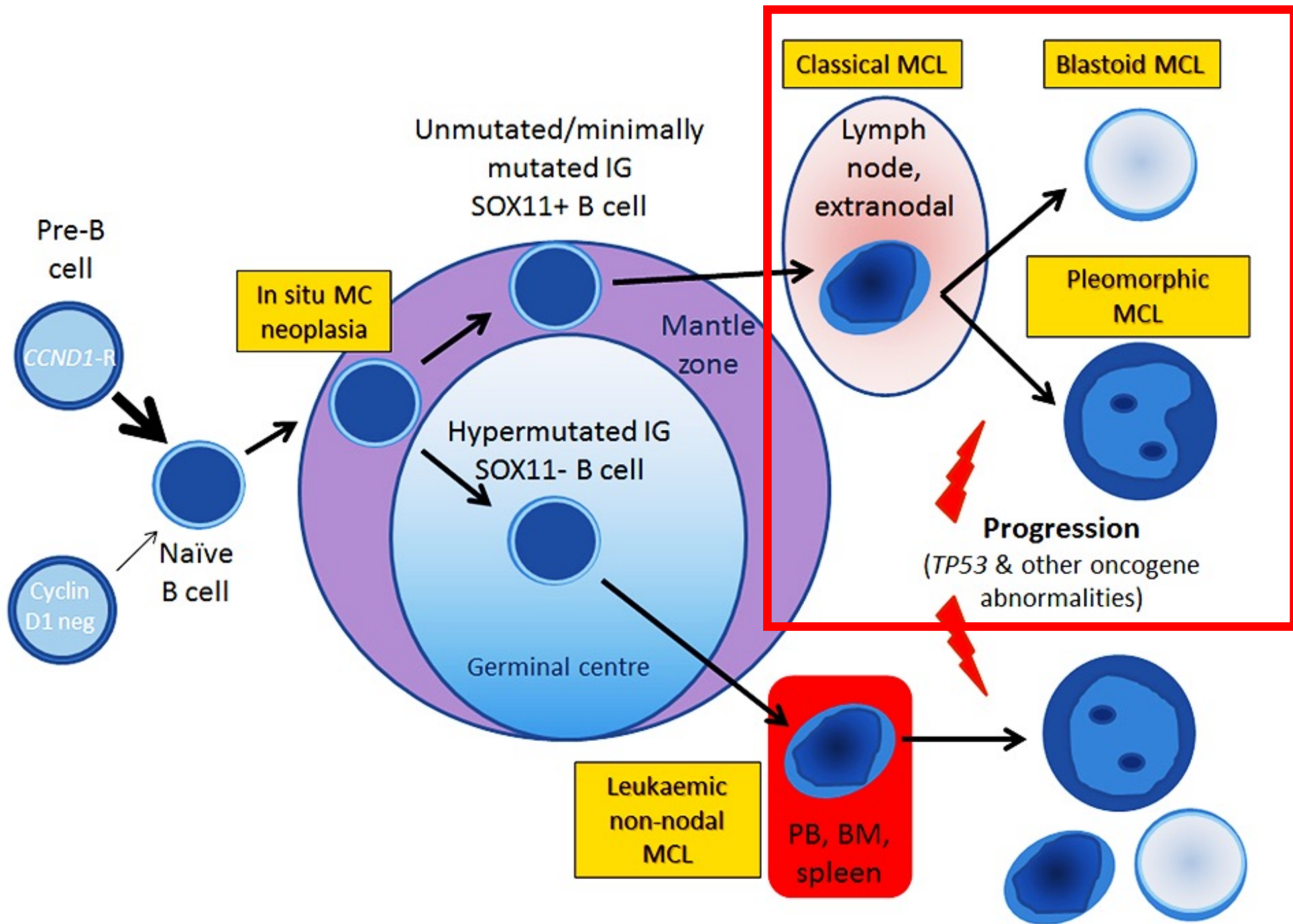


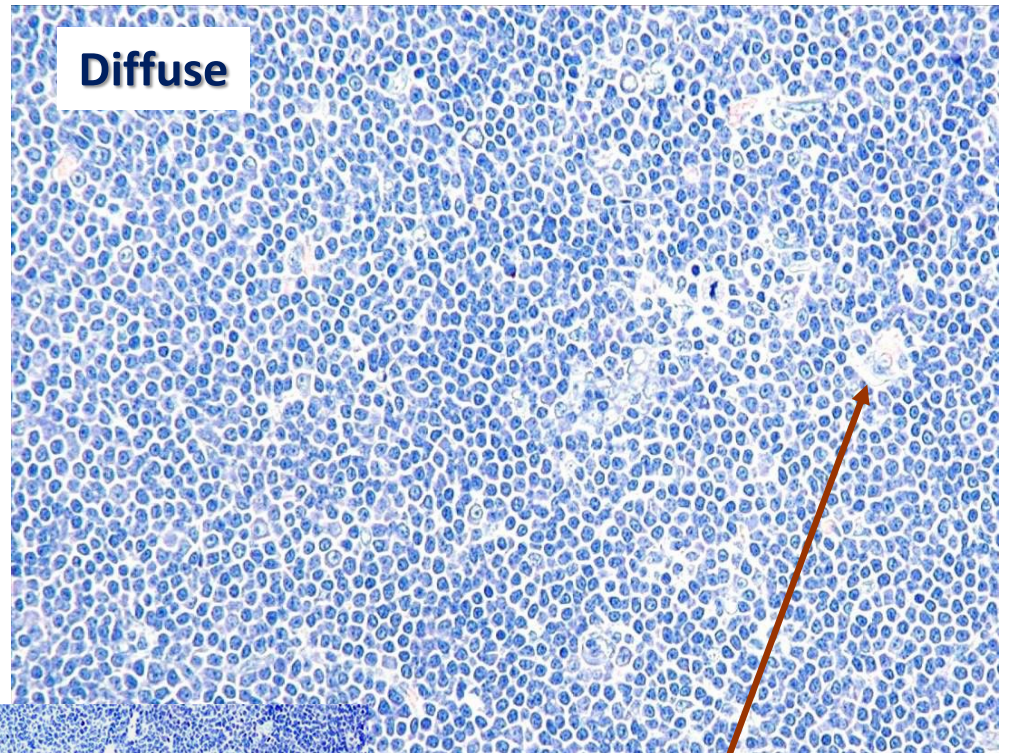
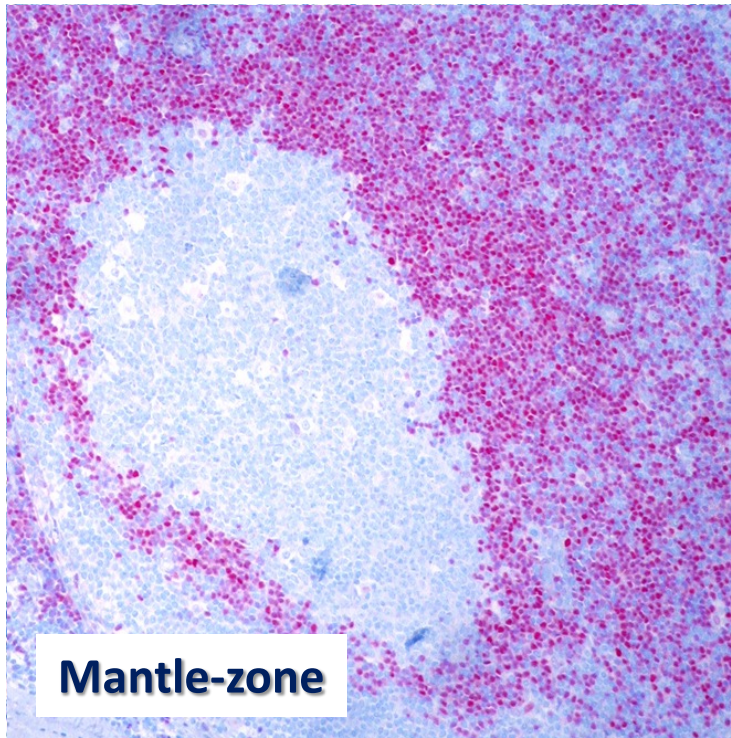


# Mantle cell lymphoma

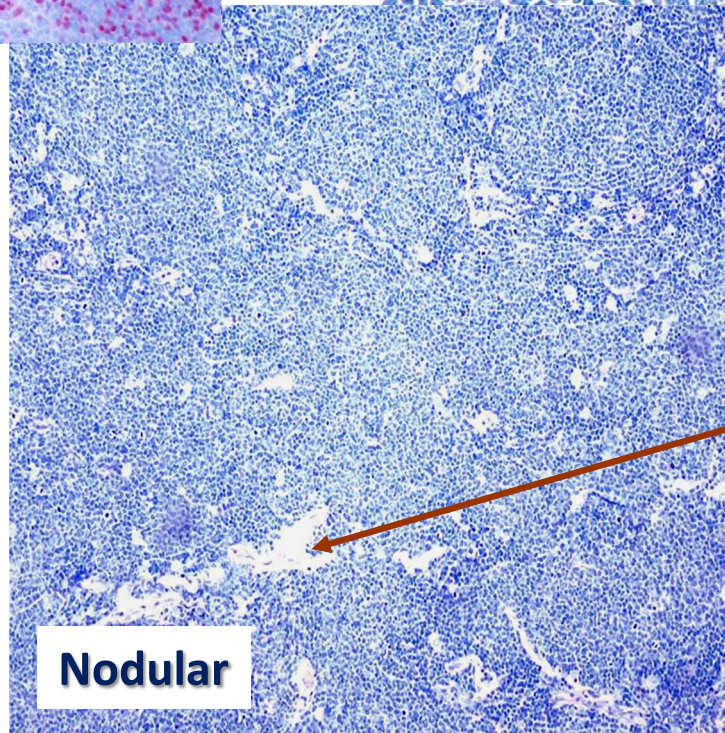
## Definition

Mantle cell lymphoma is a mature B-cell neoplasm usually composed of monomorphic small to medium-sized lymphoid cells with irregular nuclear contours; in > 95% of cases, there is a *CCND1* translocation {245,543,2219,2269,3849,4018}. Neoplastic transformed cells (centroblasts), paraimmunoblasts, and proliferation centres are absent. Mantle cell lymphoma has traditionally been considered a very aggressive and incurable lymphoma, but more indolent variants, including leukaemic non-nodal mantle cell lymphoma and in situ mantle cell neoplasia, are now also well recognized.

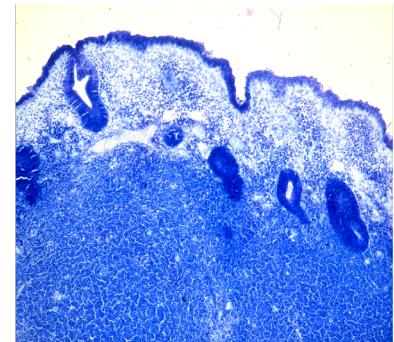


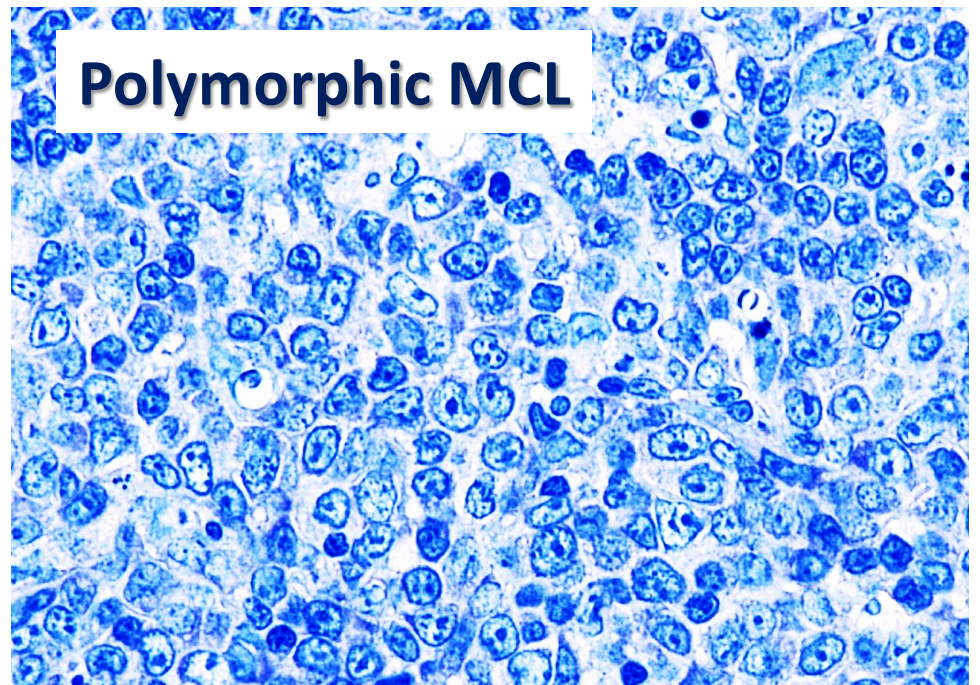
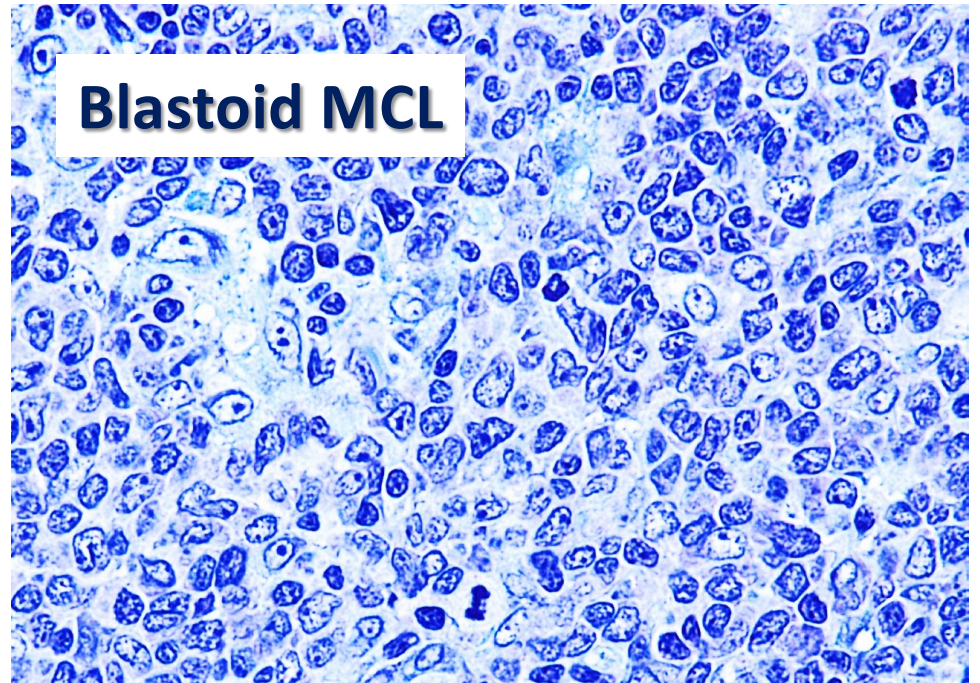
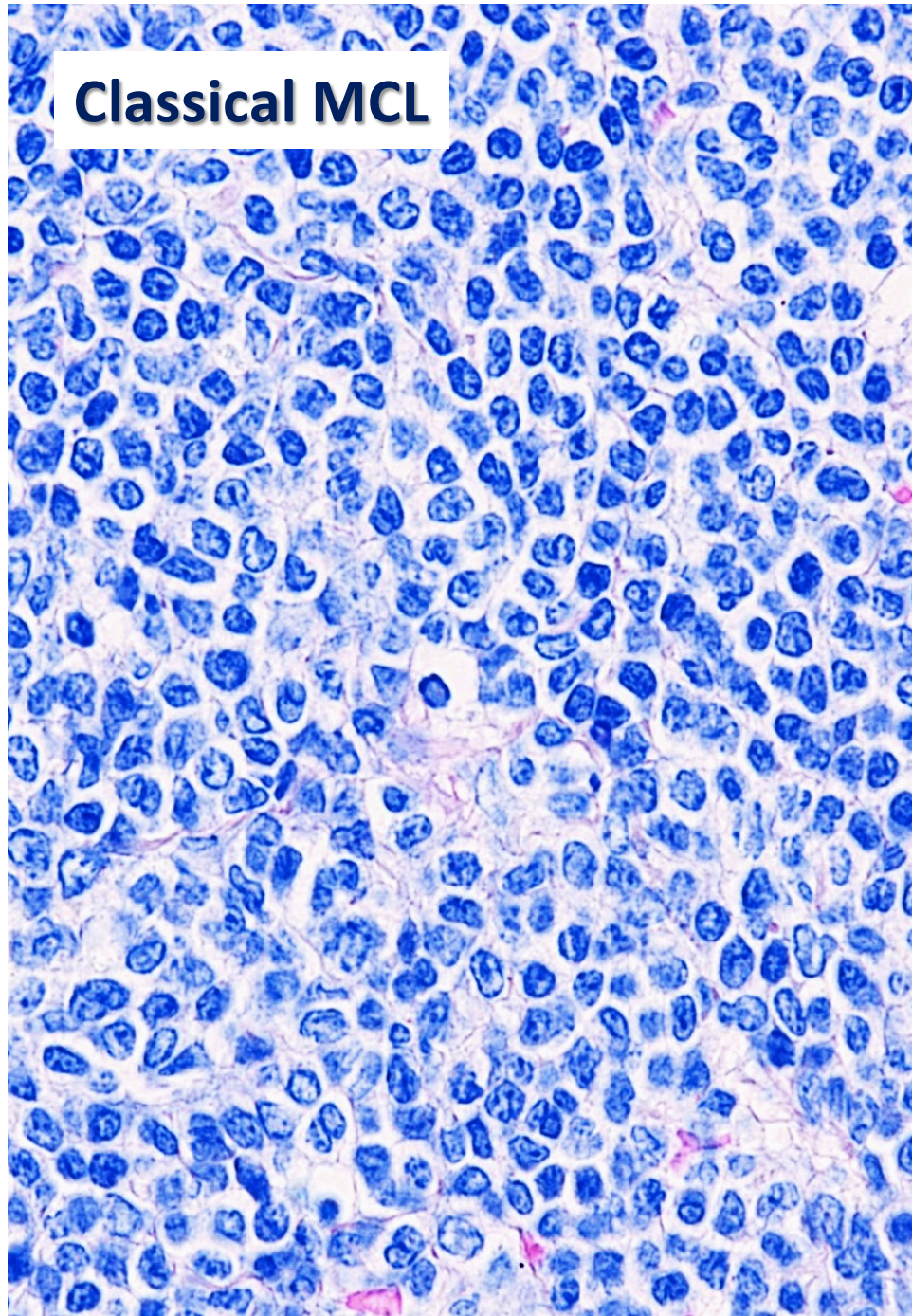


# MCL Growth Patterns



Epithelioid  
histiocytes







# Phenotype

CD19, CD20, CD22, CD79a, CD79b +

CD5+

IgM+

IgD+

Cyclin D1+ (>95%)

SOX11+ (- in leukemic non nodal)

BCL2+

CD23 -

IRF4 -

CD200 – (at times + in leukemic non nodal)

LEF1 – (at times + in blastoid/pleomorphic)

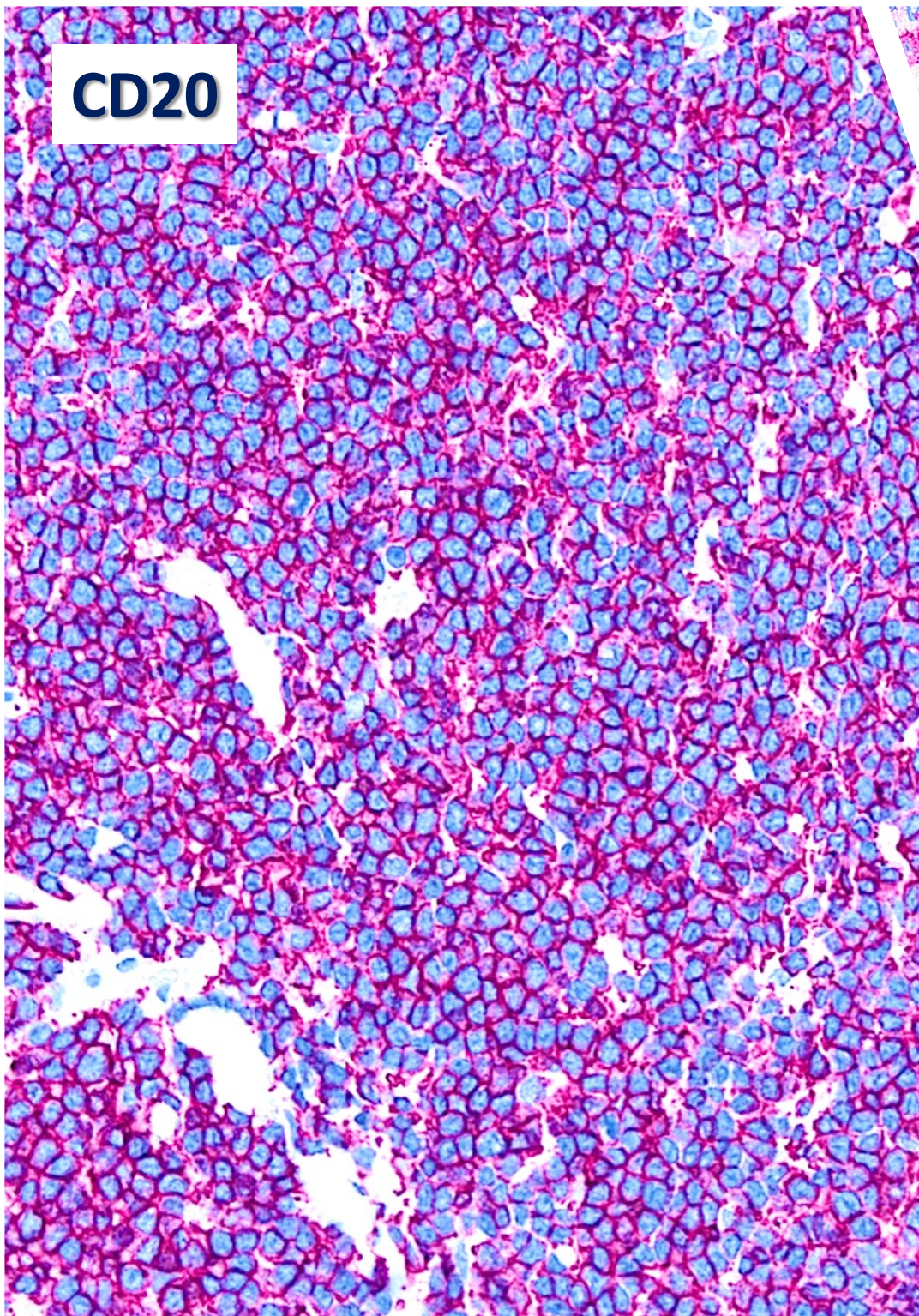
IRTA1, MNDA, T-bet -

CD10, BCL6, LMO2 –

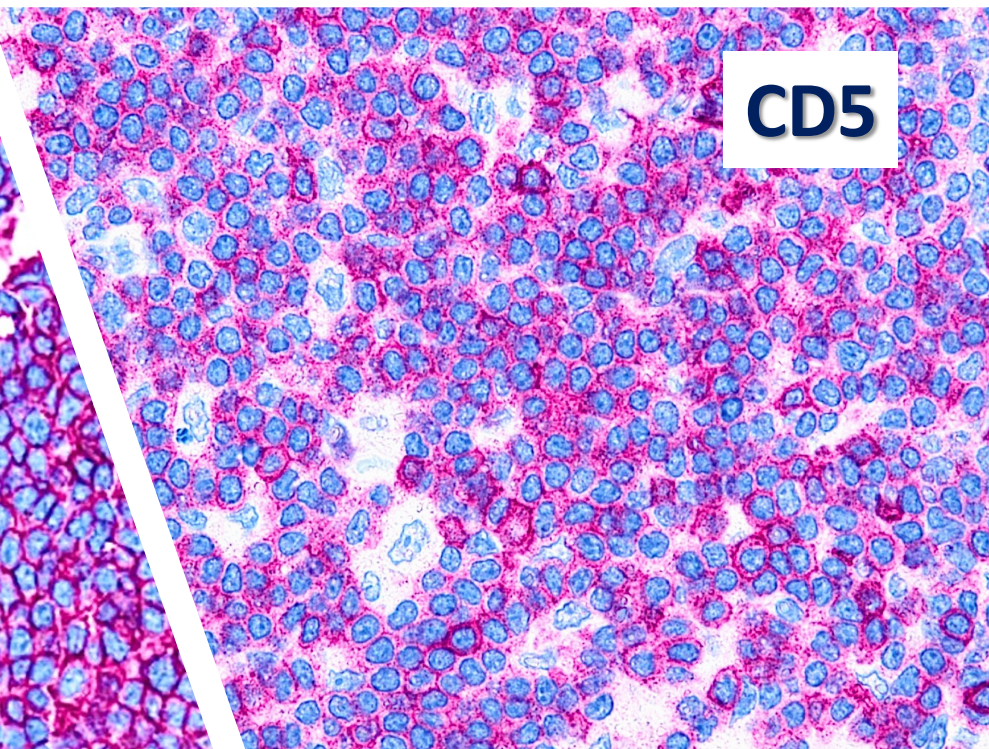
Ki-67: variable



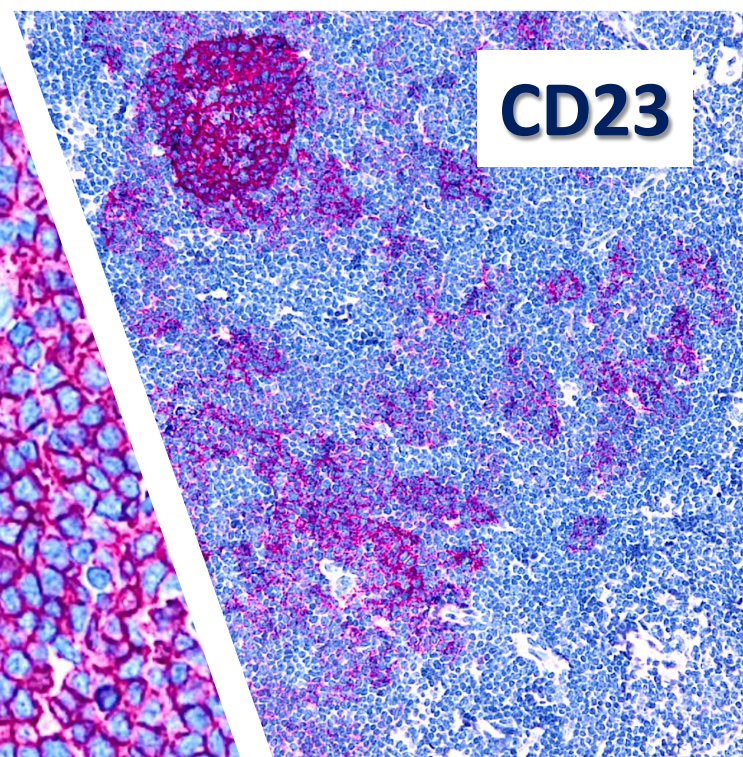
**CD20**



**CD5**



**CD23**



## LYMPHOID NEOPLASIA

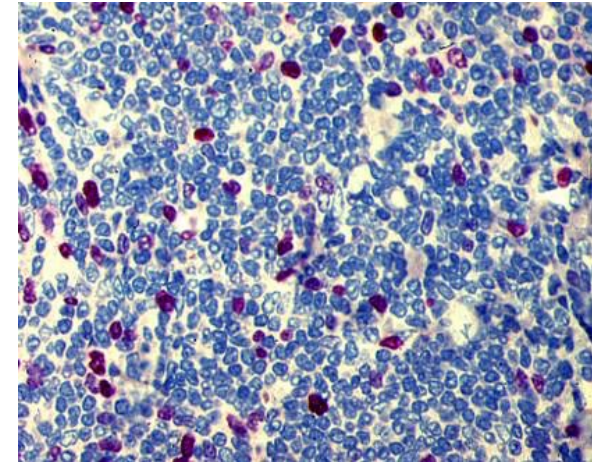
# *CCND2* and *CCND3* hijack immunoglobulin light-chain enhancers in cyclin D1<sup>-</sup> mantle cell lymphoma

David Martín-García,<sup>1,2,\*</sup> Alba Navarro,<sup>1,2,\*</sup> Rafael Valdés-Mas,<sup>3</sup> Guillem Clot,<sup>1,2</sup> Jesús Gutiérrez-Abril,<sup>3</sup> Miriam Prieto,<sup>1,2</sup> Inmaculada Ribera-Cortada,<sup>4</sup> Renata Woroniecka,<sup>5</sup> Grzegorz Rymkiewicz,<sup>6</sup> Susanne Bens,<sup>7,8</sup> Laurence de Leval,<sup>9</sup> Andreas Rosenwald,<sup>10,11</sup> Judith A. Ferry,<sup>12</sup> Eric D. Hsi,<sup>13</sup> Kai Fu,<sup>14,15</sup> Jan Delabie,<sup>16,17</sup> Dennis Weisenburger,<sup>18</sup> Daphne de Jong,<sup>19</sup> Fina Climent,<sup>20</sup> Sheila J. O'Connor,<sup>21</sup> Steven H. Swerdlow,<sup>22</sup> David Torrents,<sup>23,24</sup> Sergi Beltran,<sup>25</sup> Blanca Espinet,<sup>26,27</sup> Blanca González-Farré,<sup>2,28</sup> Luis Veloza,<sup>28</sup> Dolors Costa,<sup>2,28</sup> Estella Matutes,<sup>28</sup> Reiner Siebert,<sup>7,8</sup> German Ott,<sup>29,30</sup> Leticia Quintanilla-Martinez,<sup>31</sup> Elaine S. Jaffe,<sup>32</sup> Carlos López-Otín,<sup>2,3</sup> Itziar Salaverria,<sup>1,2</sup> Xose S. Puente,<sup>2,3,†</sup> Elias Campo,<sup>1,2,28,33,†</sup> and Sílvia Beà<sup>1,2,†</sup>

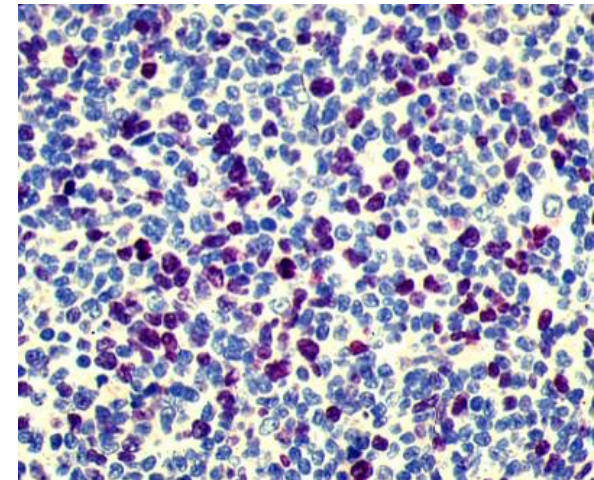
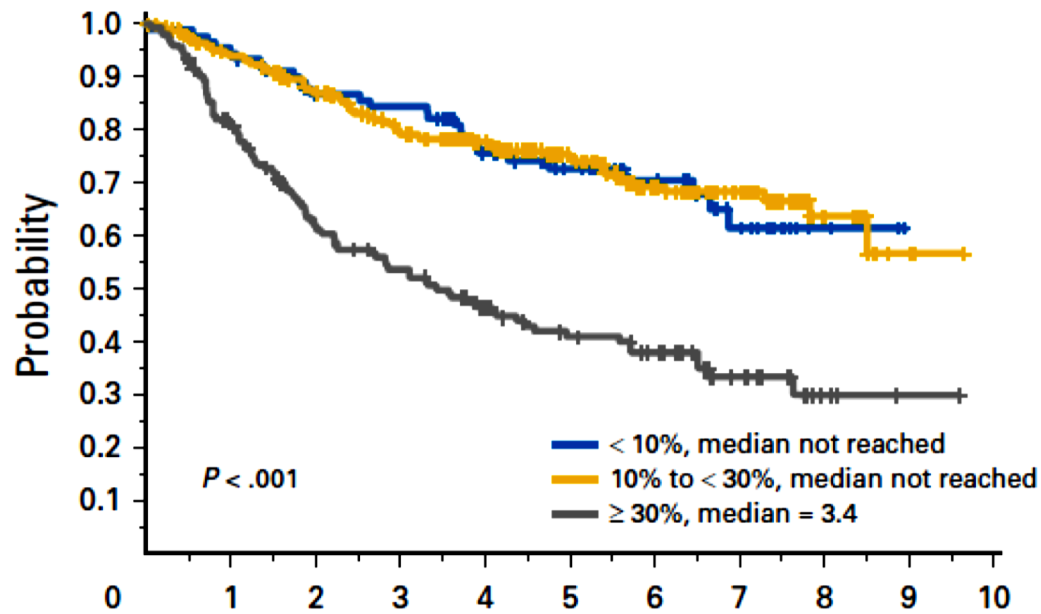
**(*Blood*. 2019;133(9):940-951)**

### Prognostic Value of Ki-67 Index, Cytology, and Growth Pattern in Mantle-Cell Lymphoma: Results From Randomized Trials of the European Mantle Cell Lymphoma Network

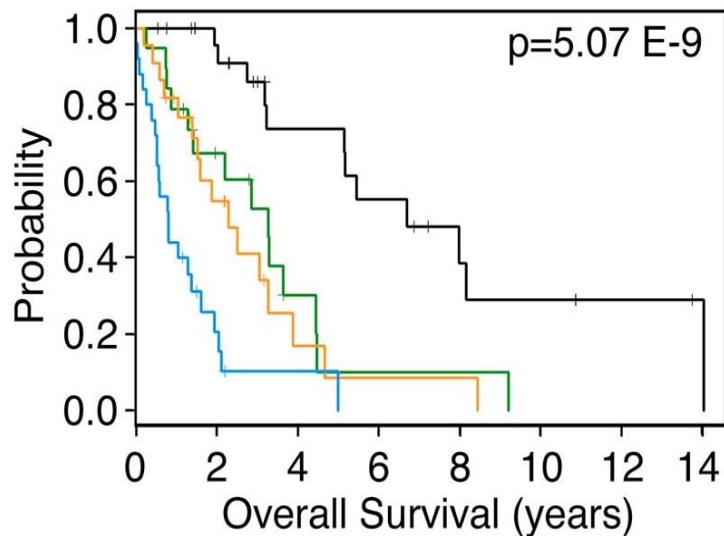
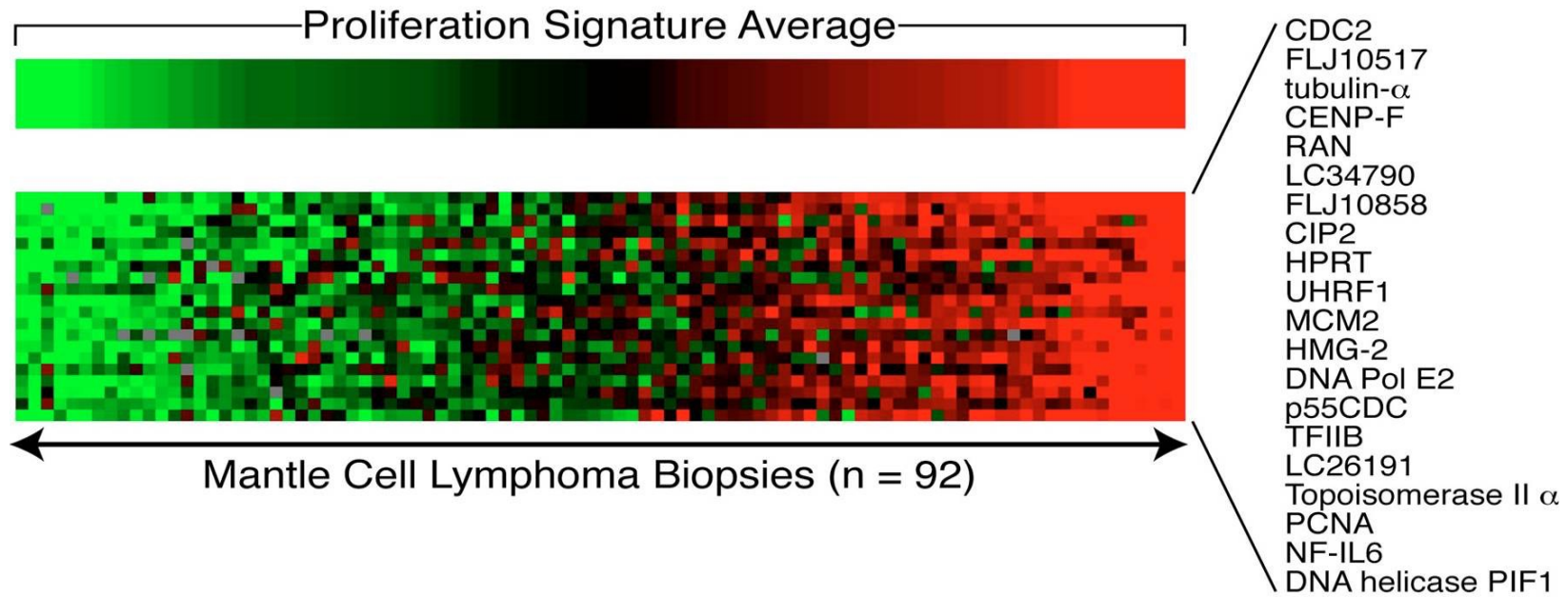
*Eva Hoster, Andreas Rosenwald, Françoise Berger, Heinz-Wolfram Bernd, Sylvia Hartmann, Christoph Loddenkemper, Thomas F.E. Barth, Nicole Brousse, Stefano Pileri, Grzegorz Rymkiewicz, Roman Kodet, Stephan Stilgenbauer, Roswitha Forstpointner, Catherine Thieblemont, Michael Hallek, Bertrand Coiffier, Ursula Vehling-Kaiser, Réda Bouabdallah, Lothar Kanz, Michael Pfreundschuh, Christian Schmidt, Vincent Ribrag, Wolfgang Hiddemann, Michael Unterhalt, Johanna C. Kluijn-Nelemans, Olivier Hermine, Martin H. Dreyling, and Wolfram Klapper*



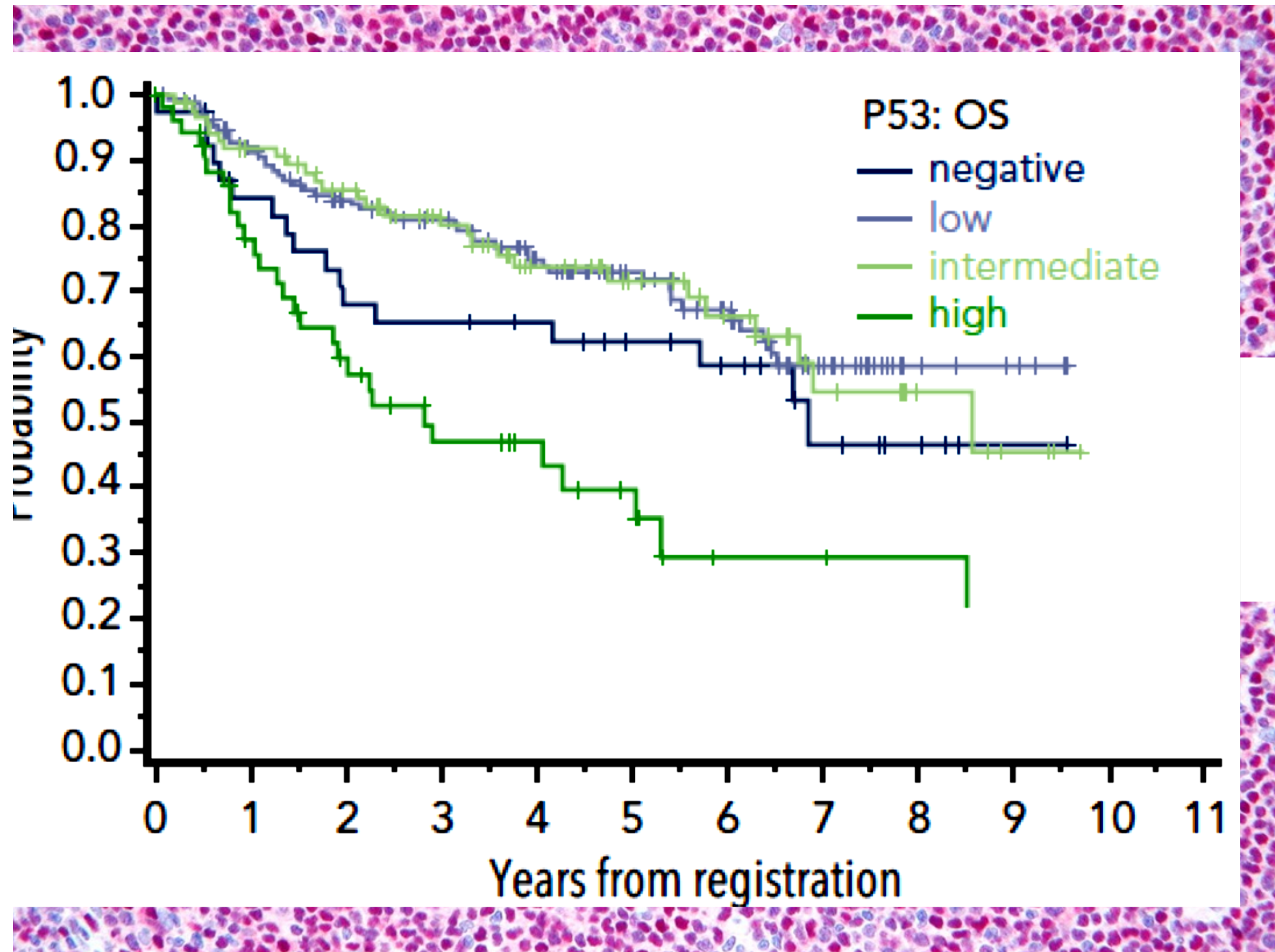
**Ki-67 index**



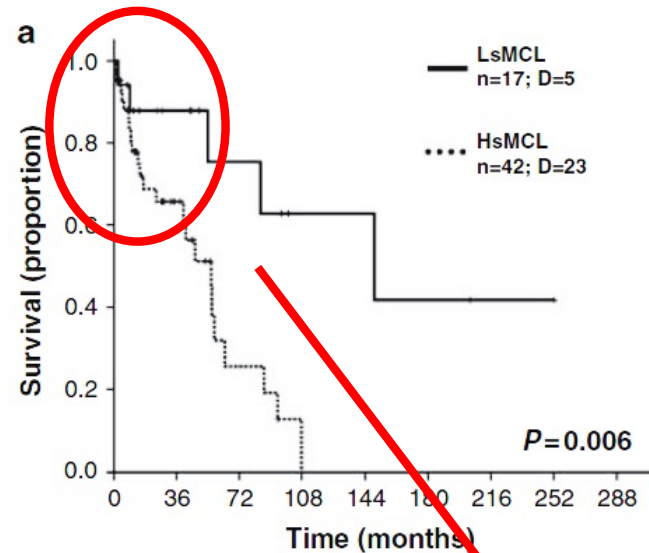
# Variable Expression of Proliferation Signature Genes in Mantle Cell Lymphoma



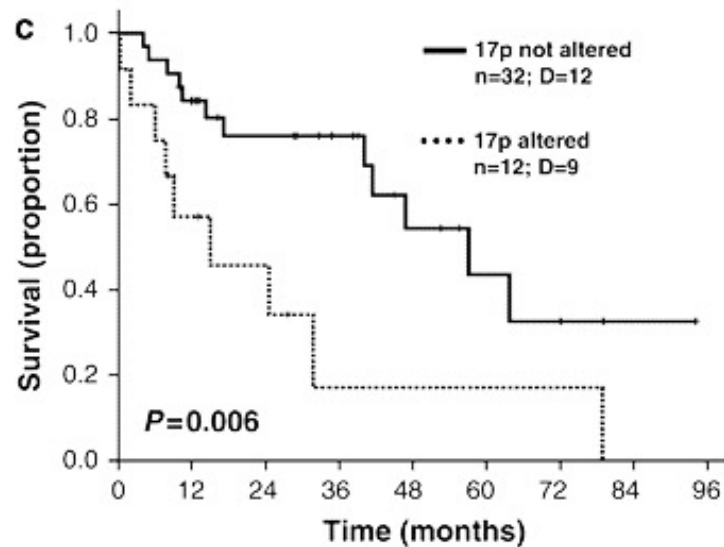
**Rosenwald A et LLMP, Cancer Cell 2003;  
3(2):185-97.**



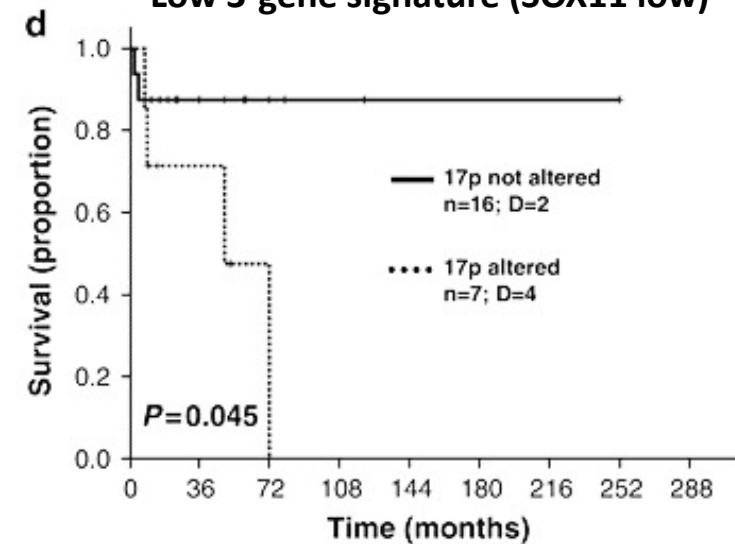
# Prognostic impact of 17p del and *TP53* mutations in MCL

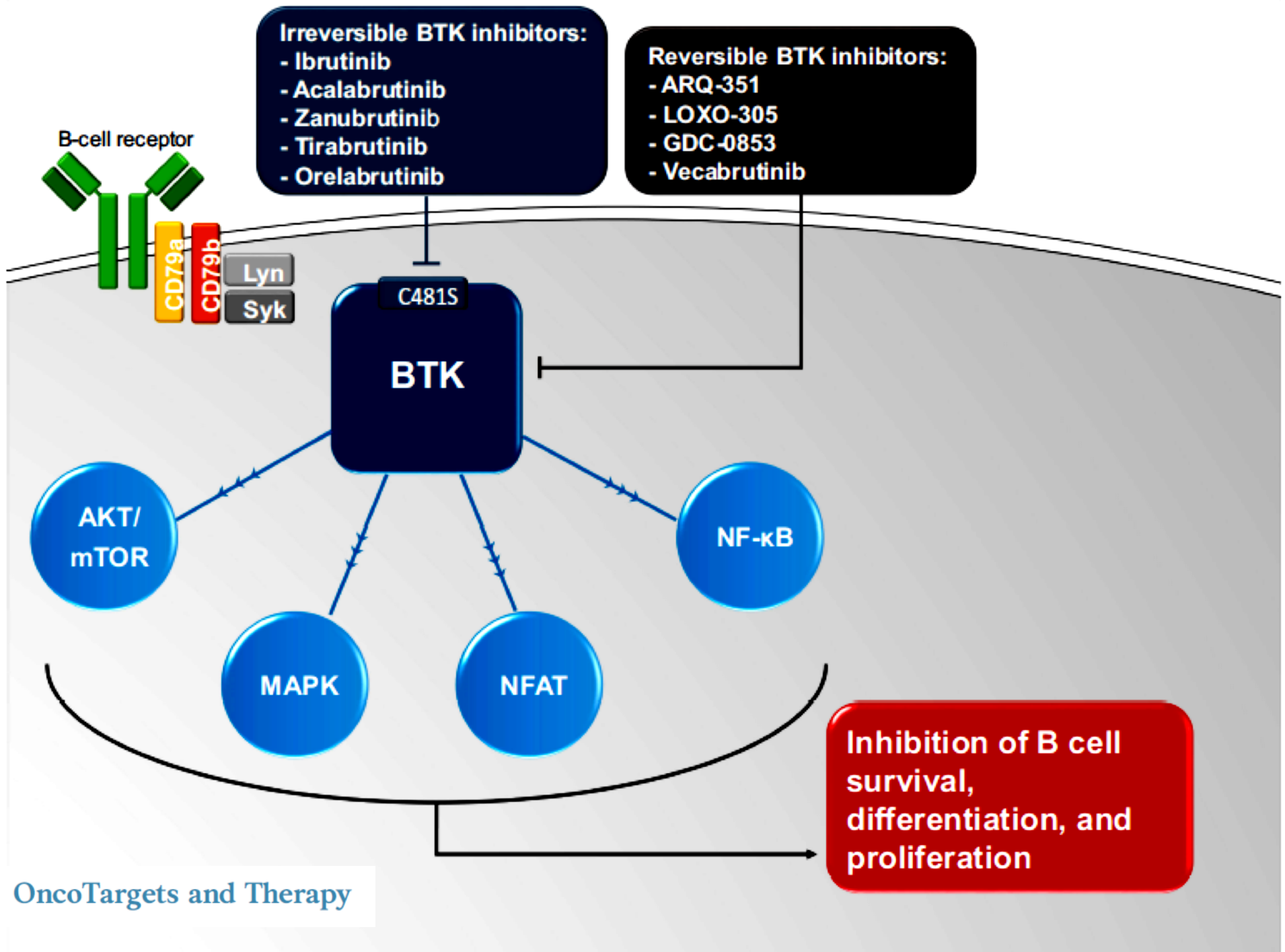


High 3-gene signature (SOX11high)

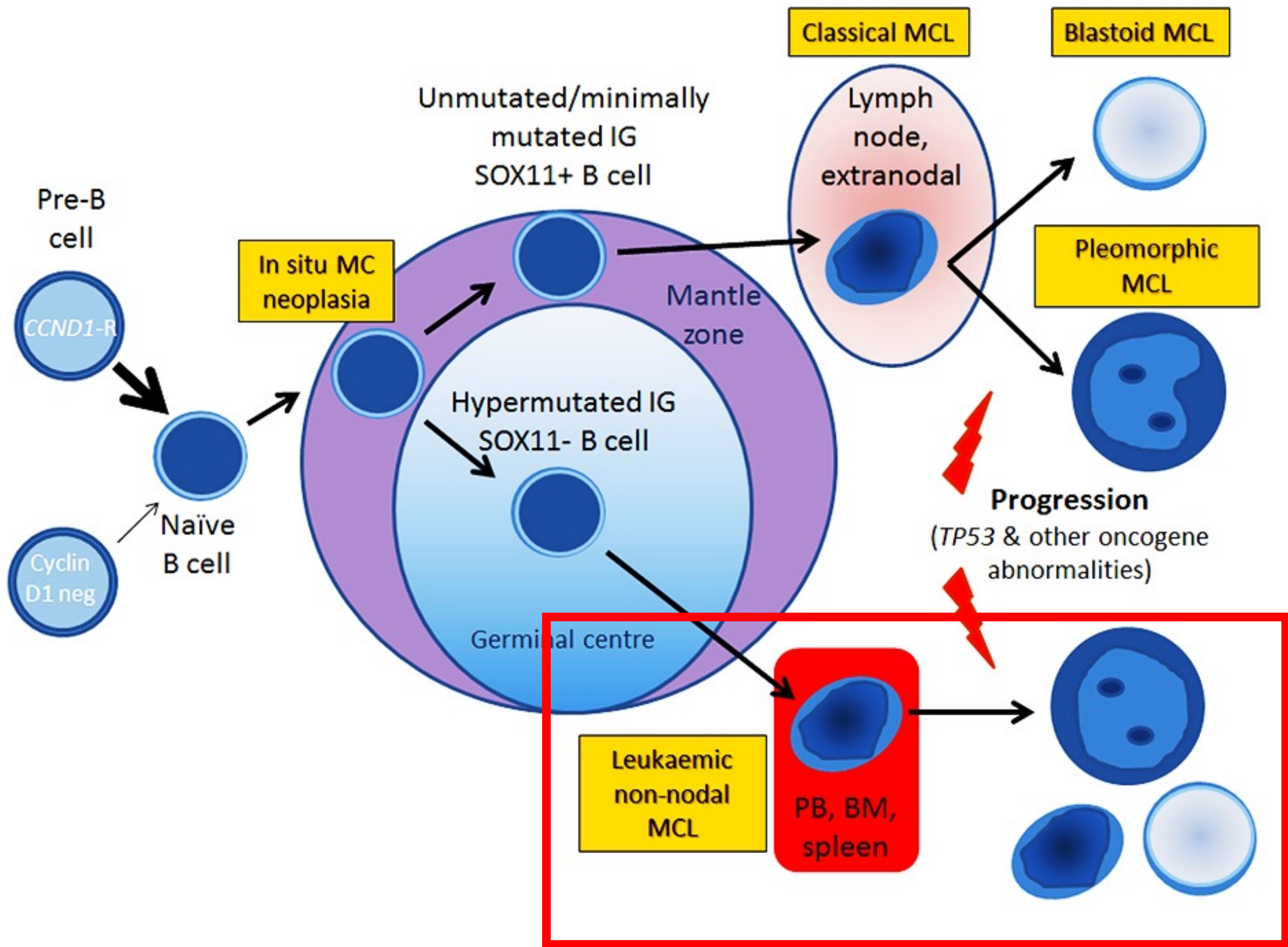


Low 3-gene signature (SOX11 low)









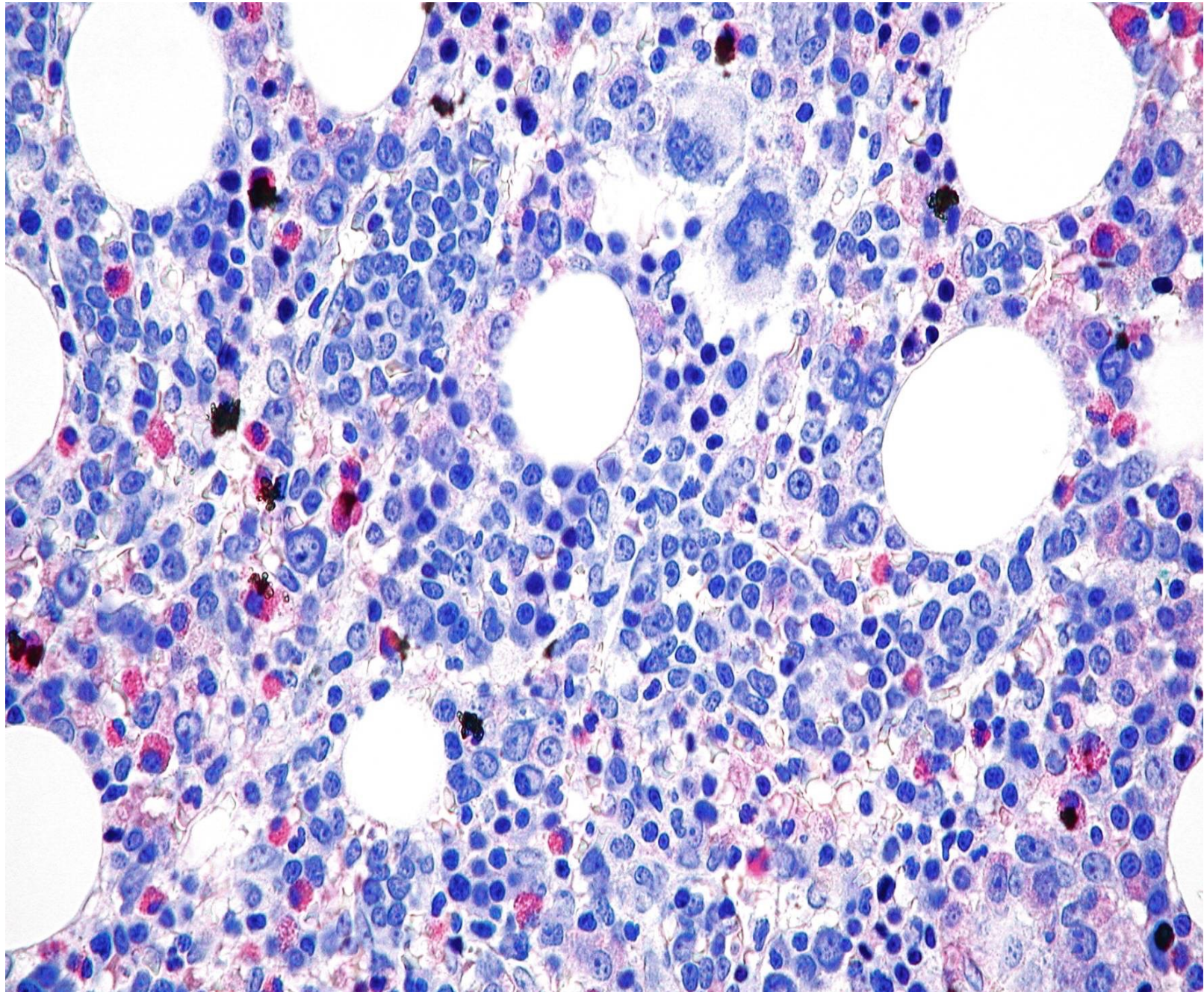
## **Genomic and Gene Expression Profiling Defines Indolent Forms of Mantle Cell Lymphoma**

Verònica Fernández<sup>1</sup>, Olga Salamero<sup>2</sup>, Blanca Espinet<sup>3</sup>, Francesc Solé<sup>3</sup>, Cristina Royo<sup>1</sup>, Alba Navarro<sup>1</sup>, Francisca Camacho<sup>4</sup>, Silvia Beà<sup>1</sup>, Elena Hartmann<sup>5</sup>, Virginia Amador<sup>1</sup>, Luis Hernández<sup>1</sup>, Claudio Agostinelli<sup>6</sup>, Rachel L. Sargent<sup>7</sup>, Maria Rozman<sup>1</sup>, Marta Aymerich<sup>1</sup>, Dolors Colomer<sup>1</sup>, Neus Villamor<sup>1</sup>, Steven H. Swerdlow<sup>7</sup>, Stefano A. Pileri<sup>6</sup>, Francesc Bosch<sup>2</sup>, Miguel A. Piris<sup>4</sup>, Emili Montserrat<sup>2</sup>, German Ott<sup>8</sup>, Andreas Rosenwald<sup>5</sup>, Armando López-Guillermo<sup>2</sup>, Pedro Jares<sup>1</sup>, Sergi Serrano<sup>3</sup>, and Elías Campo<sup>1</sup>

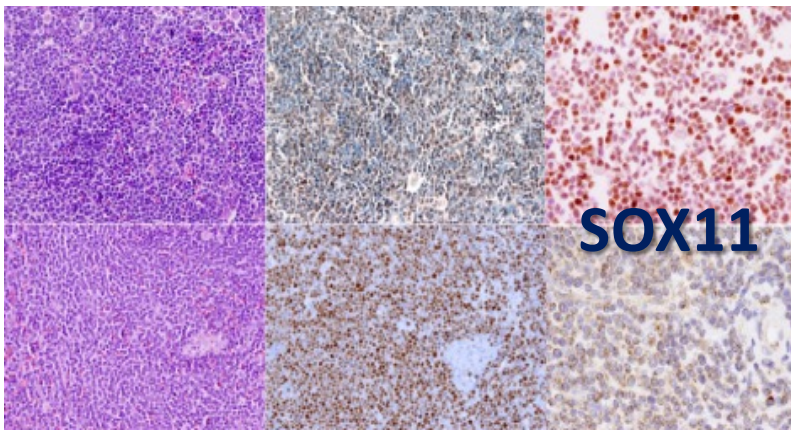
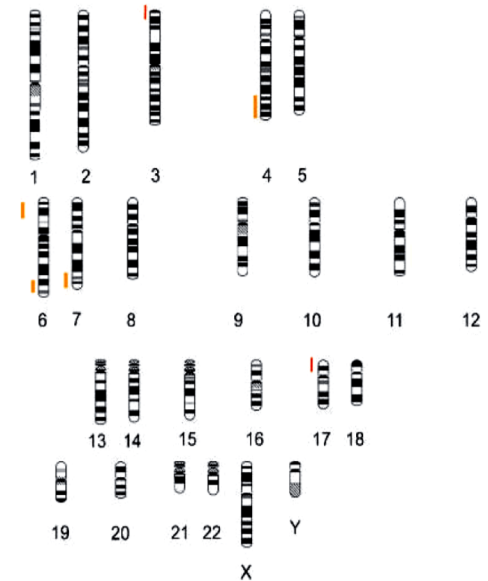
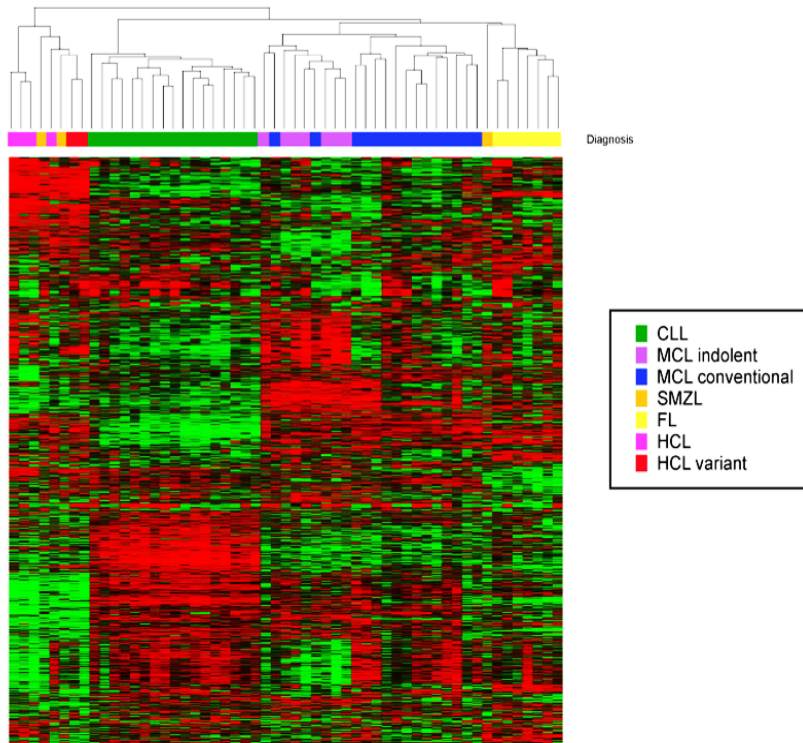
## **Molecular Subsets of Mantle Cell Lymphoma Defined by the *IGHV* Mutational Status and SOX11 Expression Have Distinct Biologic and Clinical Features**

Alba Navarro<sup>1</sup>, Guillem Clot<sup>1</sup>, Cristina Royo<sup>1</sup>, Pedro Jares<sup>1</sup>, Anastasia Hadzidimitriou<sup>4</sup>, Andreas Agathangelidis<sup>4,5</sup>, Vasilis Bikos<sup>4</sup>, Nikos Darzentas<sup>4</sup>, Theodora Papadaki<sup>7</sup>, Itziar Salaverria<sup>1,8</sup>, Magda Pinyol<sup>1</sup>, Xavier Puig<sup>2</sup>, Jara Palomero<sup>1</sup>, Maria Carmela Vegliante<sup>1</sup>, Virginia Amador<sup>1</sup>, Alejandra Martinez-Trillos<sup>1</sup>, Lenka Stefancikova<sup>12</sup>, Adrian Wiestner<sup>13</sup>, Wyndham Wilson<sup>13</sup>, Christiane Pott<sup>9</sup>, Maria Jose Calasanz<sup>3</sup>, Nicola Trim<sup>14</sup>, Wendy Erber<sup>15</sup>, Birgitta Sander<sup>16</sup>, German Ott<sup>10</sup>, Andreas Rosenwald<sup>11</sup>, Dolors Colomer<sup>1</sup>, Eva Giné<sup>1</sup>, Reiner Siebert<sup>8</sup>, Armando Lopez-Guillermo<sup>1</sup>, Kostas Stamatopoulos<sup>4,6</sup>, Silvia Beà<sup>1</sup>, and Elías Campo<sup>1</sup>

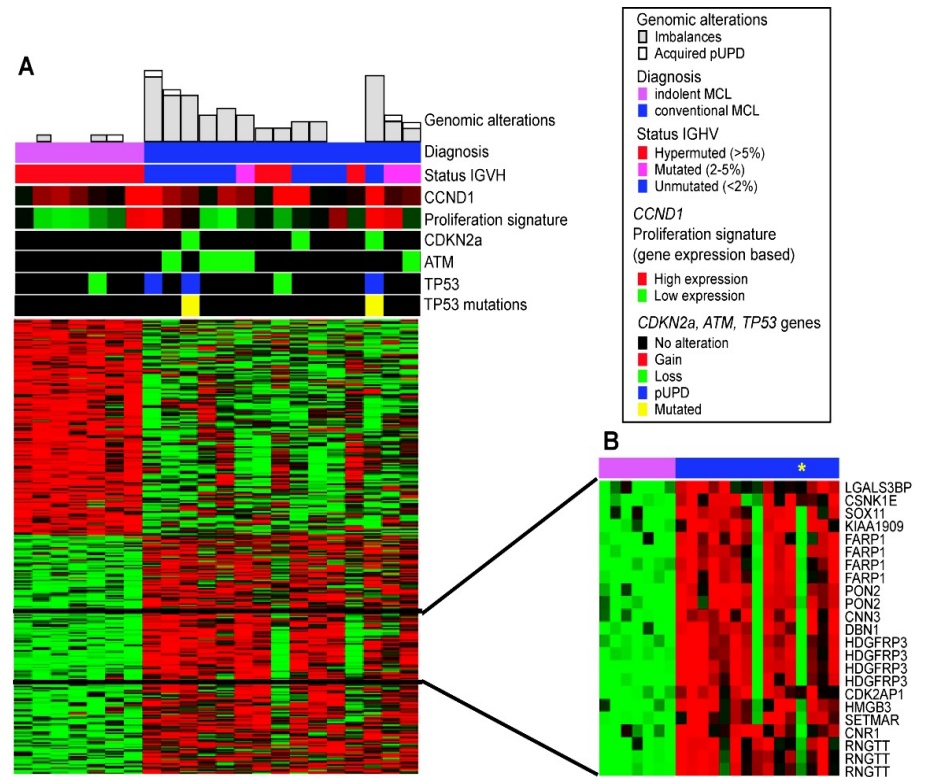
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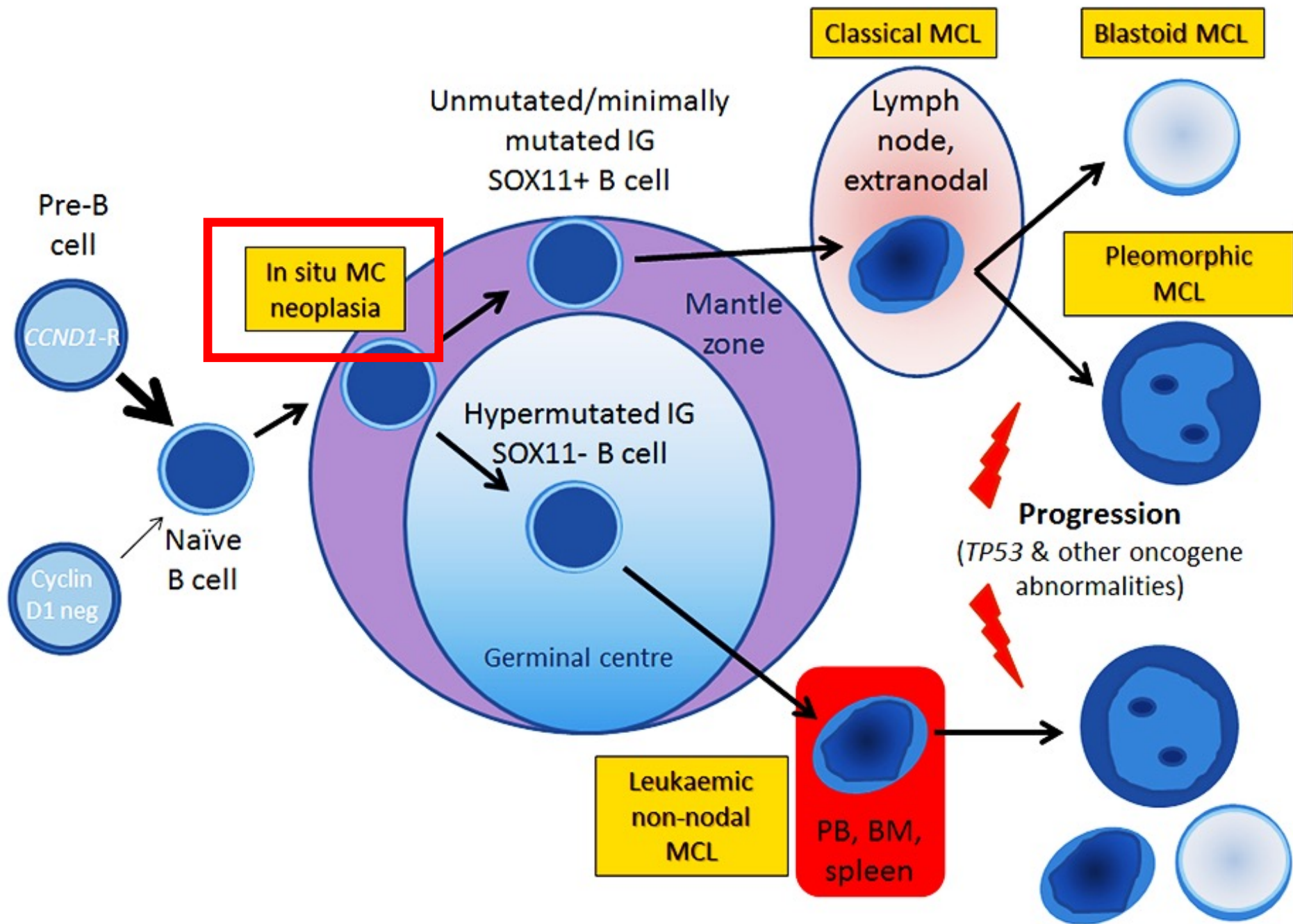


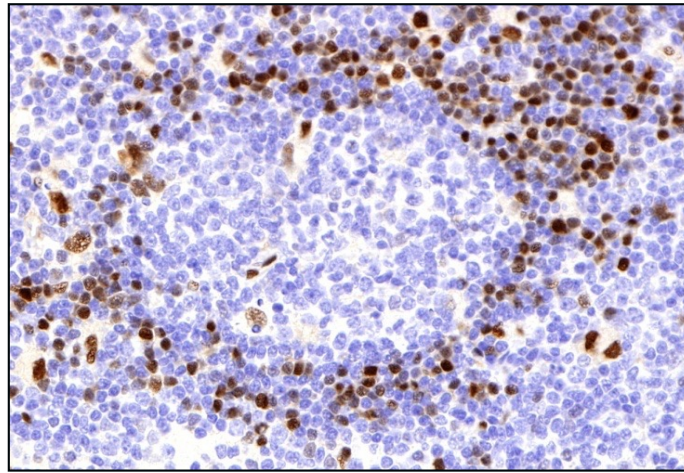
	<b>cMCL (n=15)</b>	<b>iMCL (n=12)</b>	<b>P value</b>
B symptoms (%)	33	0	0.03
Non-ambulatory performance status ECOG≥2 (%)	70	0	0.01
<b>Nodal presentation (lymph nodes &gt;1 cm) (%)*</b>	<b>93</b>	<b>17</b>	<b>&lt;0.001</b>
High serum LDH* (%)	46	0	0.03
Intermediate or high-risk MIPI	46	0	0.016
Morphology	13	67	0.007
Small cell (%)	74	33	
Classical	13	-	
Blastoid			
<b><i>IGHV</i> gene hypermutations (&gt;5%)</b>	<b>20</b>	<b>70</b>	<b>&lt; 0.04</b>
<b>Genomic Profile</b>			
<b>1. imbalance</b>	<b>13</b>	<b>100</b>	<b>&lt;0.001</b>
<b>≥ 2 imbalances</b>	<b>87</b>	<b>0</b>	
Chemotherapy at any time (%)	100	17	
<b>Dead patients (%)</b>	<b>47</b>	<b>0</b>	<b>&lt;0.001</b>
5-year overall survival (%)	49	100	0.03



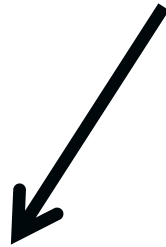
**LNMCL shows a specific gene signature and SOX11 negativity**







LN with Cyclin D1+  
In Situ Pattern



SOX11 negative

May be CD5 negative  
Rare event: <1% of LNs  
Low risk of Progression (<10%)

SOX11 positive

More often CD5 positive  
Higher risk of progression  
Similar pattern can be seen  
at relapse or at distant sites

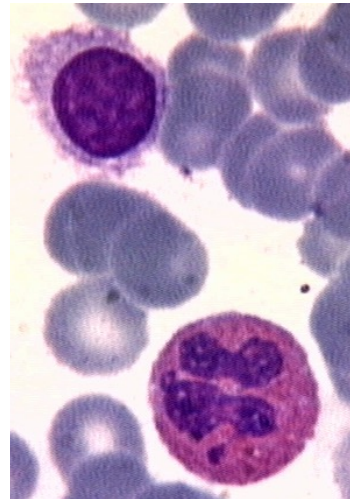
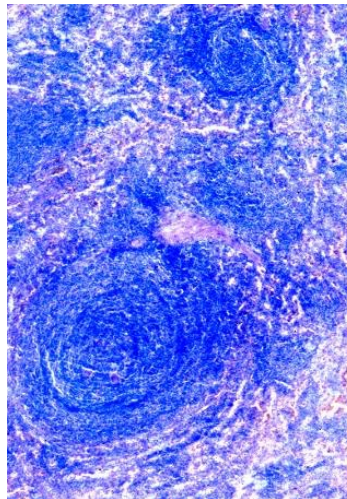
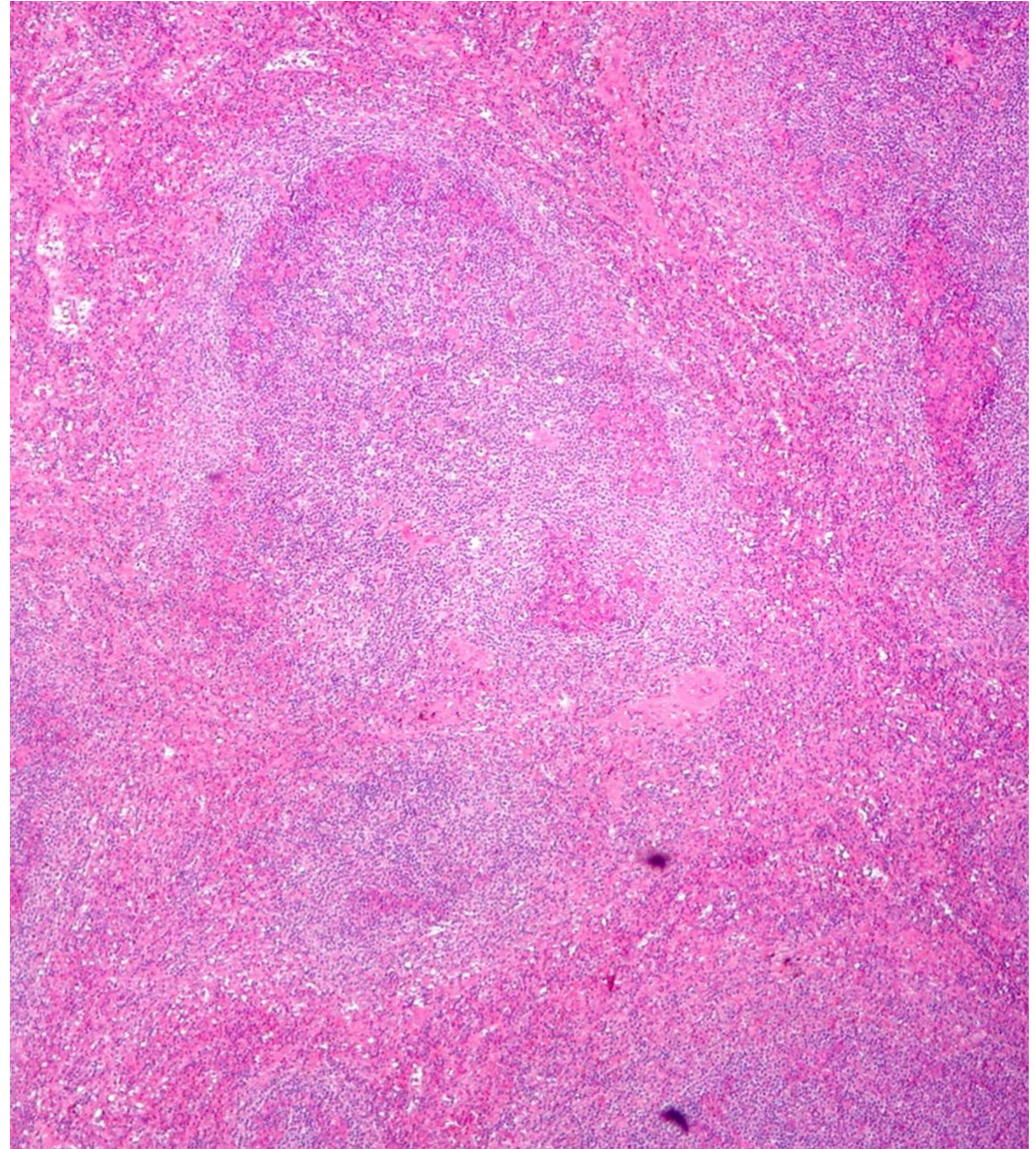
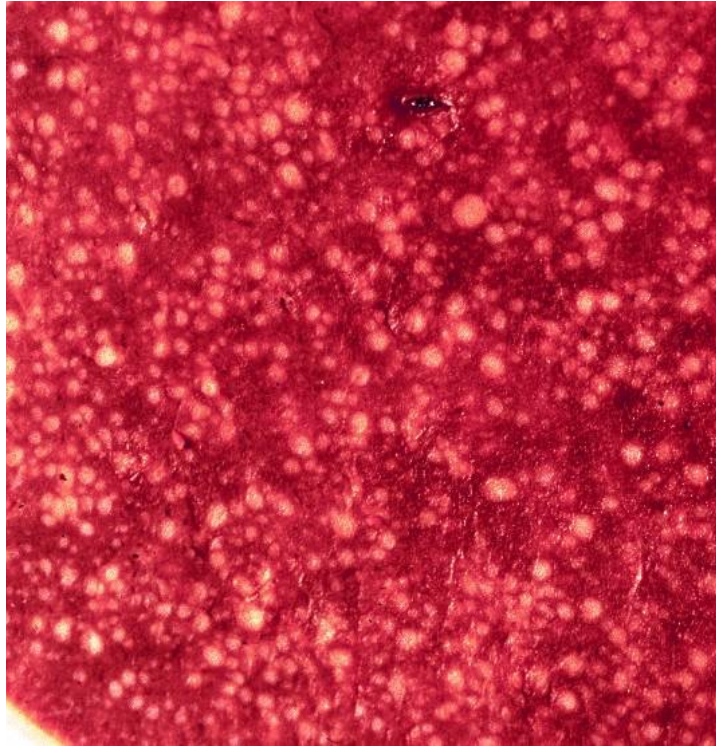
## **Splenic marginal zone lymphoma**

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### **Definition**

Splenic marginal zone lymphoma (SMZL) is a B-cell neoplasm composed of small lymphocytes that surround and replace the splenic white pulp germinal centres, efface the follicle mantle, and merge with a peripheral (marginal) zone of larger cells, including scattered transformed blasts; both small and larger cells infiltrate the red pulp. Splenic hilar lymph nodes and bone marrow are often involved; lymphoma cells are frequently found in the peripheral blood as villous lymphocytes.





# Phenotype

CD19, CD20, CD22, CD79a, CD79b +

IgM+

IgD+

MNDA+

DBA44+/-

IRF4 -/+

BCL2+ (weak)

Annexin A-

CD5- (exceptions)

CD23-

Cyclin D1 –

SOX11-

CD200 –

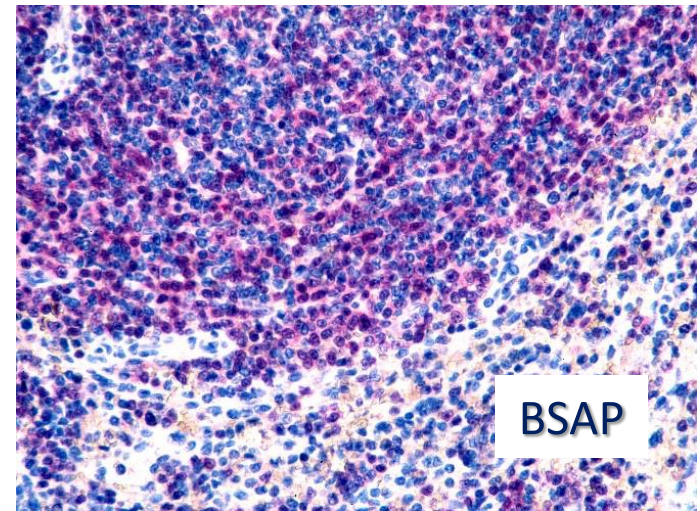
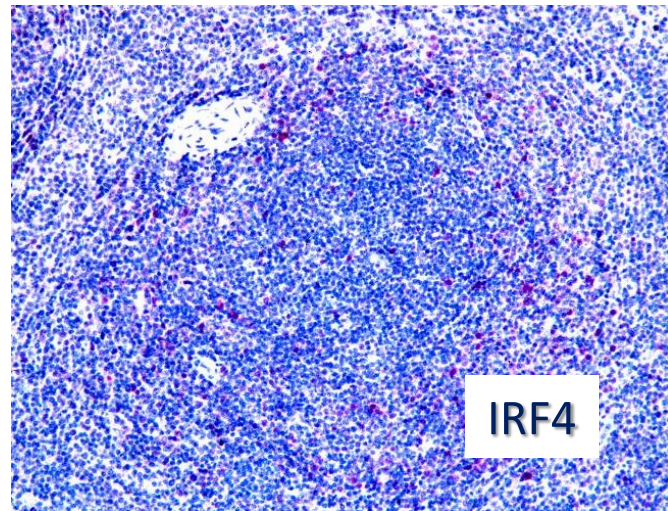
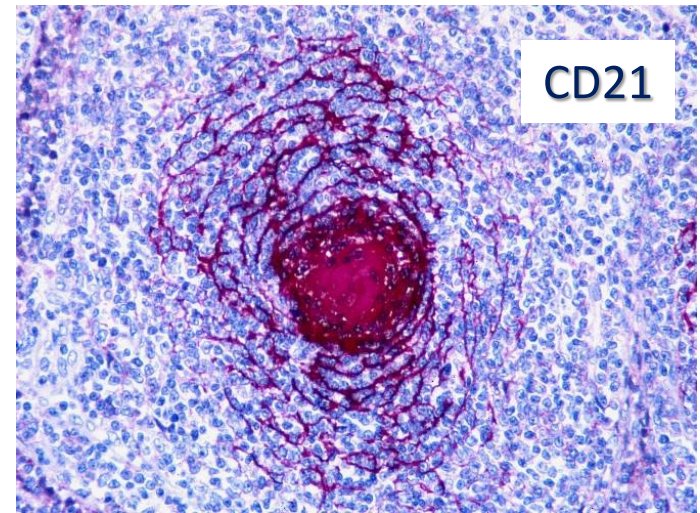
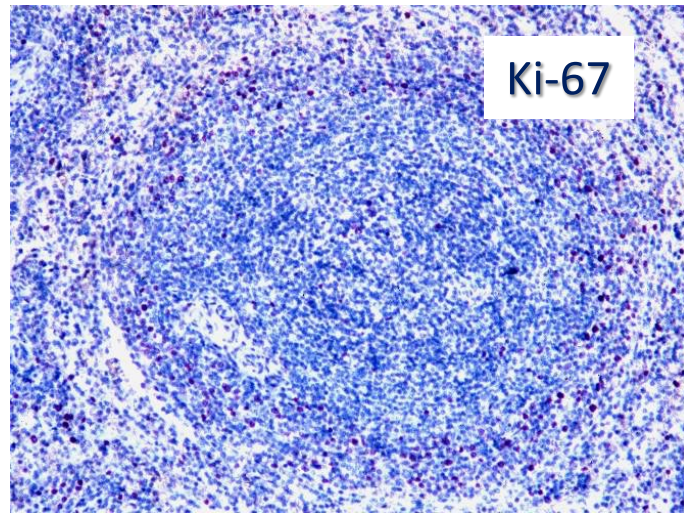
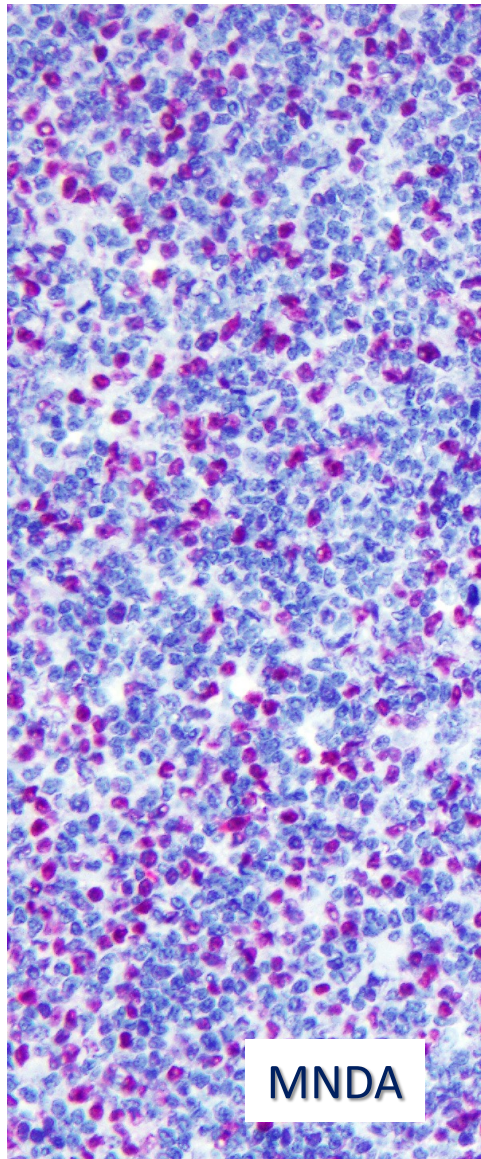
LEF1 –

IRTA1, T-bet -

CD10, BCL6, LMO2 –

Ki-67: variable



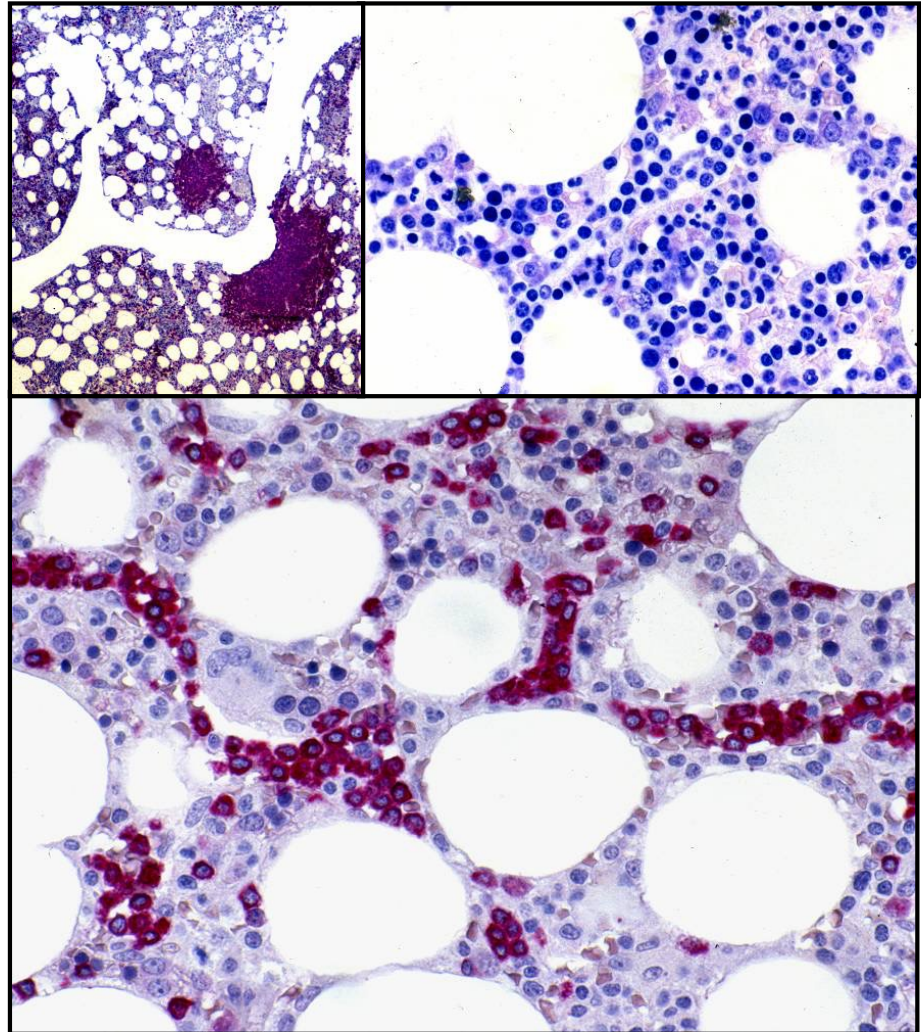


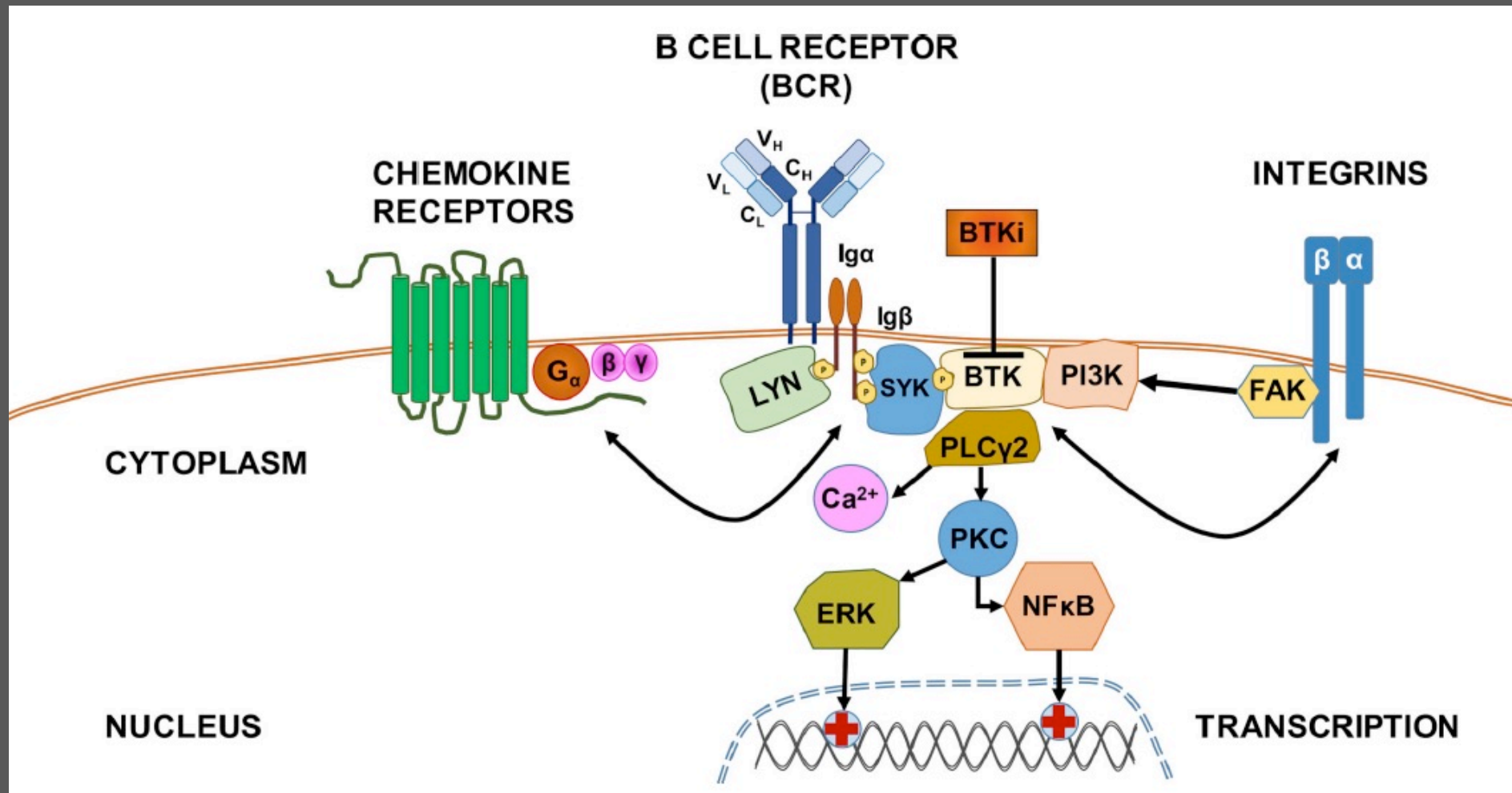
## BM involvement

nodular,

Interstitial.

Intra-sinusoidal

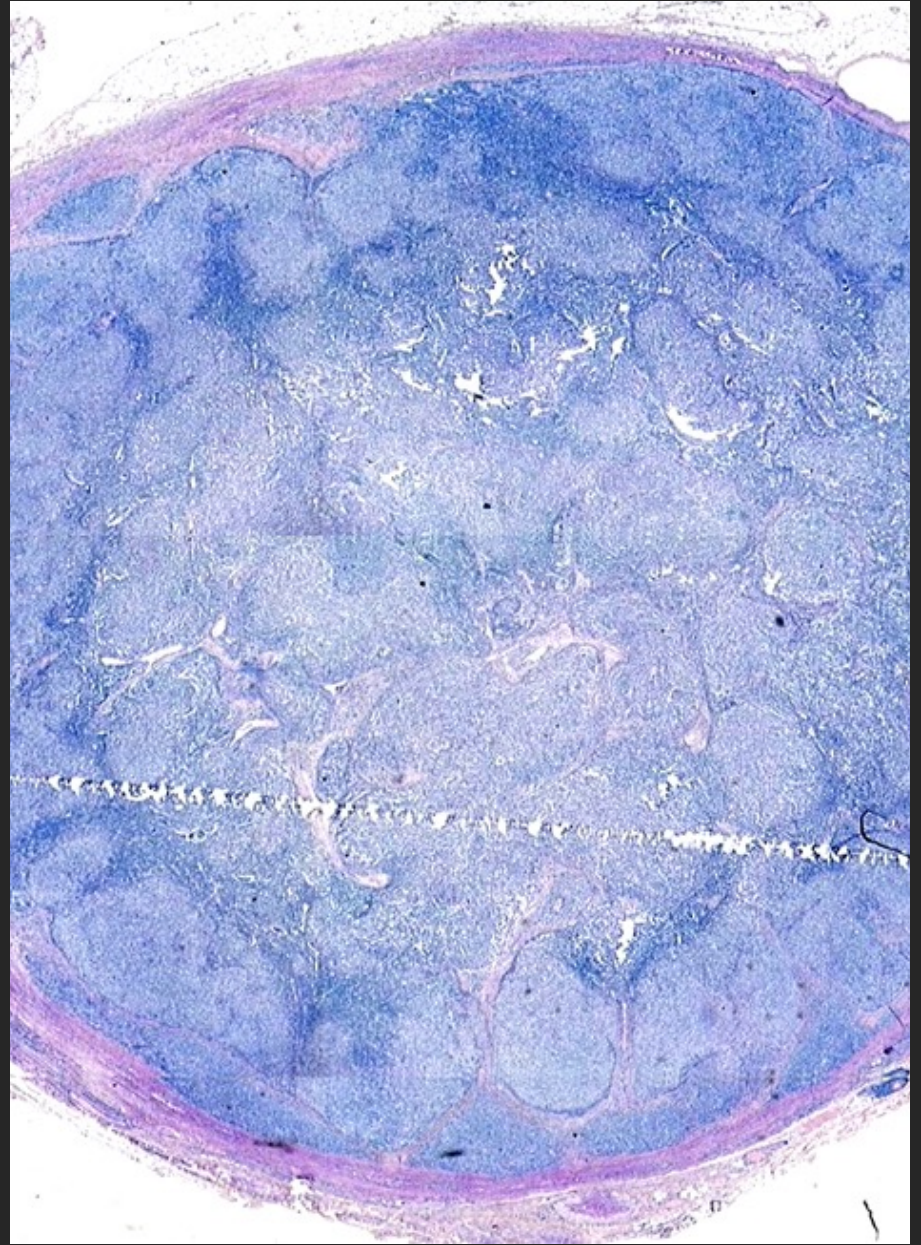
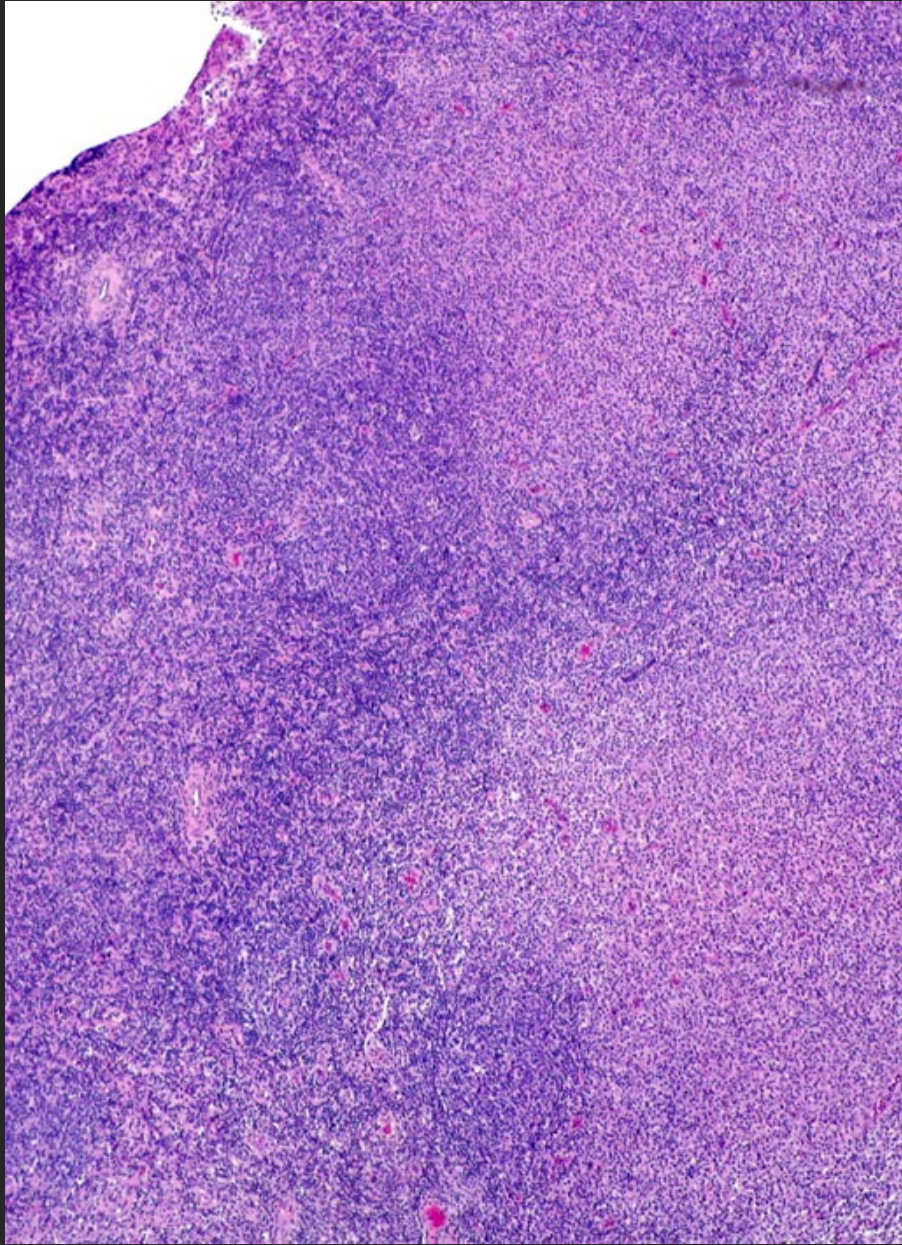


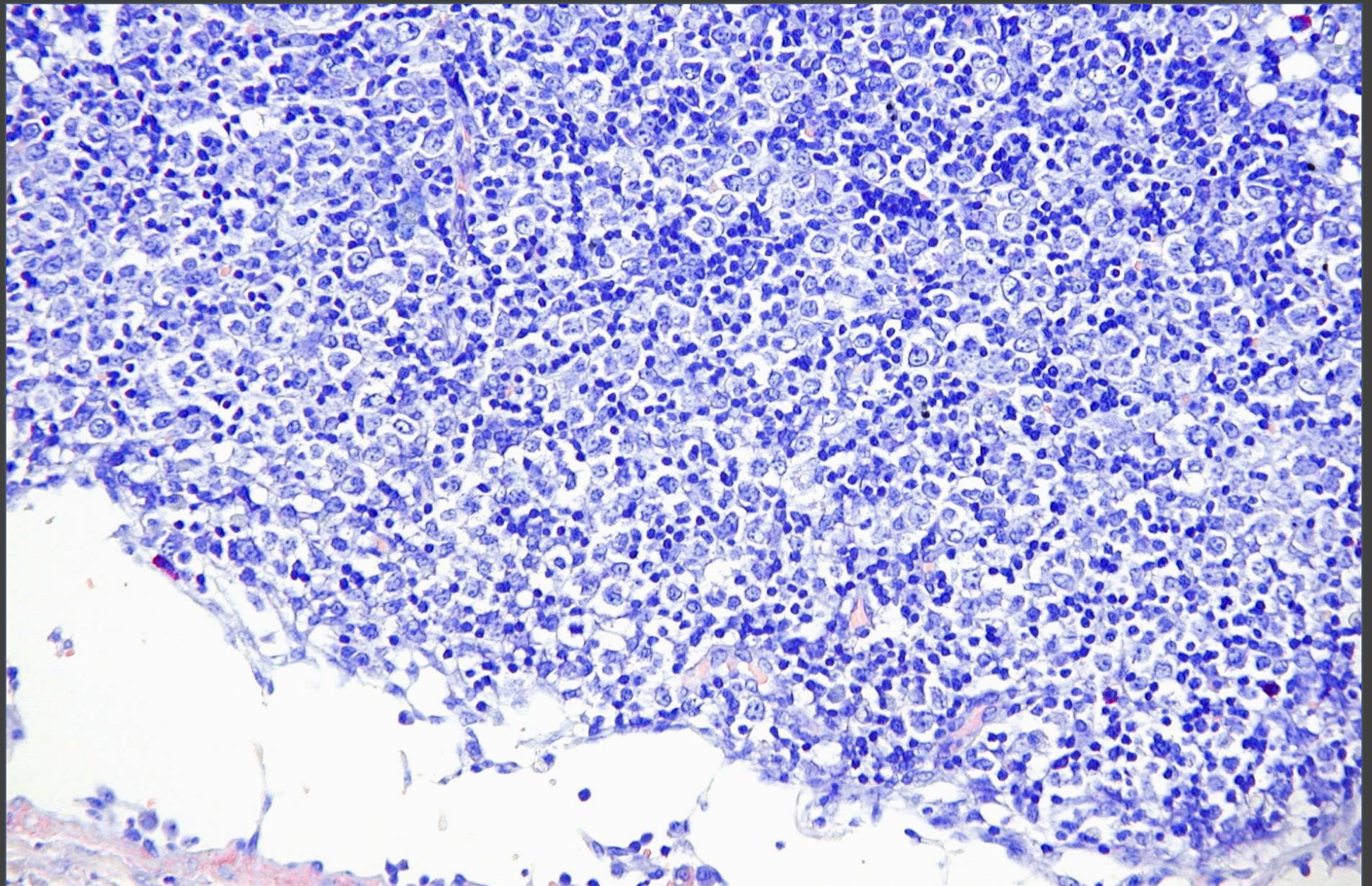


## **Nodal marginal zone lymphoma**

### **Definition**

Nodal marginal zone lymphoma (NMZL) is a primary nodal B-cell neoplasm that morphologically resembles lymph nodes involved by marginal zone lymphoma (MZL) of the extranodal or splenic types, but without evidence of extranodal or splenic disease.







# Phenotype

CD19, CD20, CD22, CD79a, CD79b +

IgM/G+

IgD-/+

**IRTA1+, T-bet+ (monocytoid); MNDA+ (splenic-type)**

IRF4-/+ (plasma cell differentiation)

BCL2+ (weak)

CD5- (rarely +)

CD23-

Cyclin D1 –

SOX11-

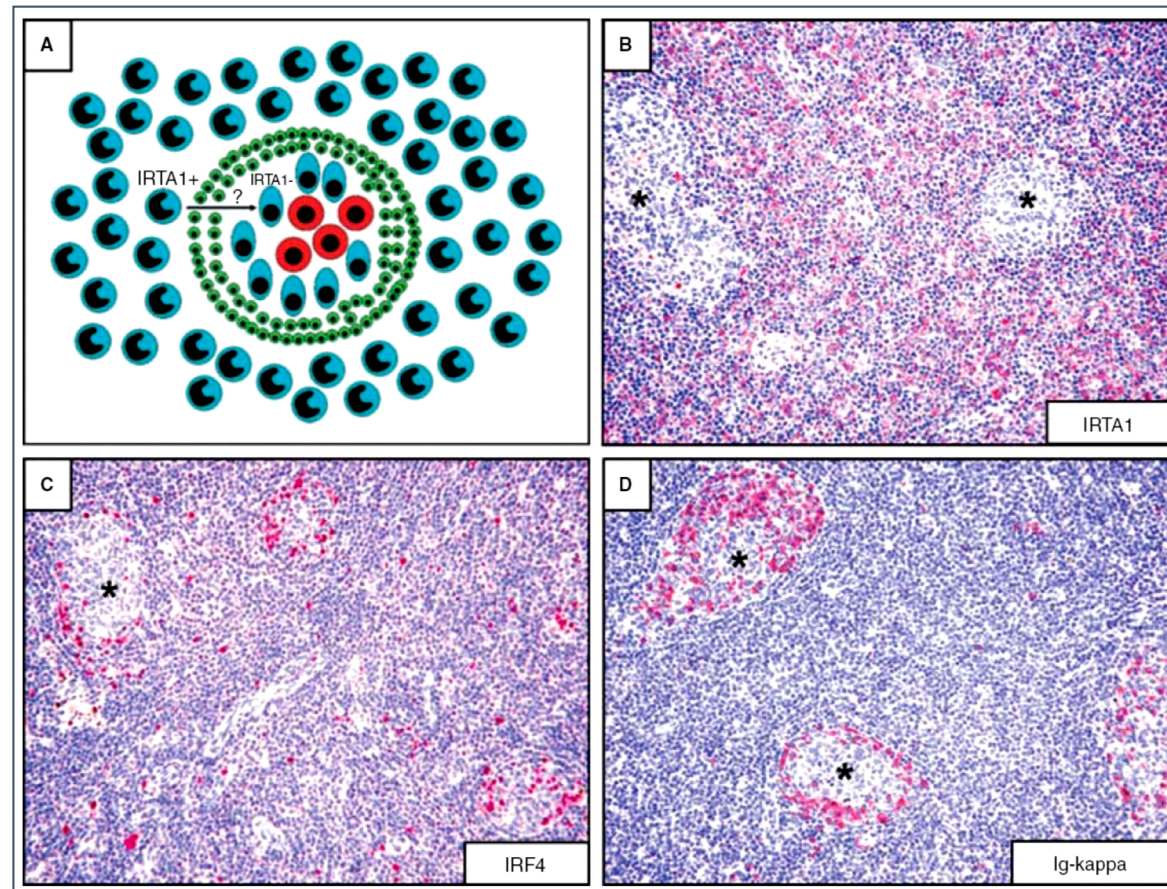
CD200 –

LEF1 –

CD10, BCL6 (colonization), LMO2 –

Ki-67: variable

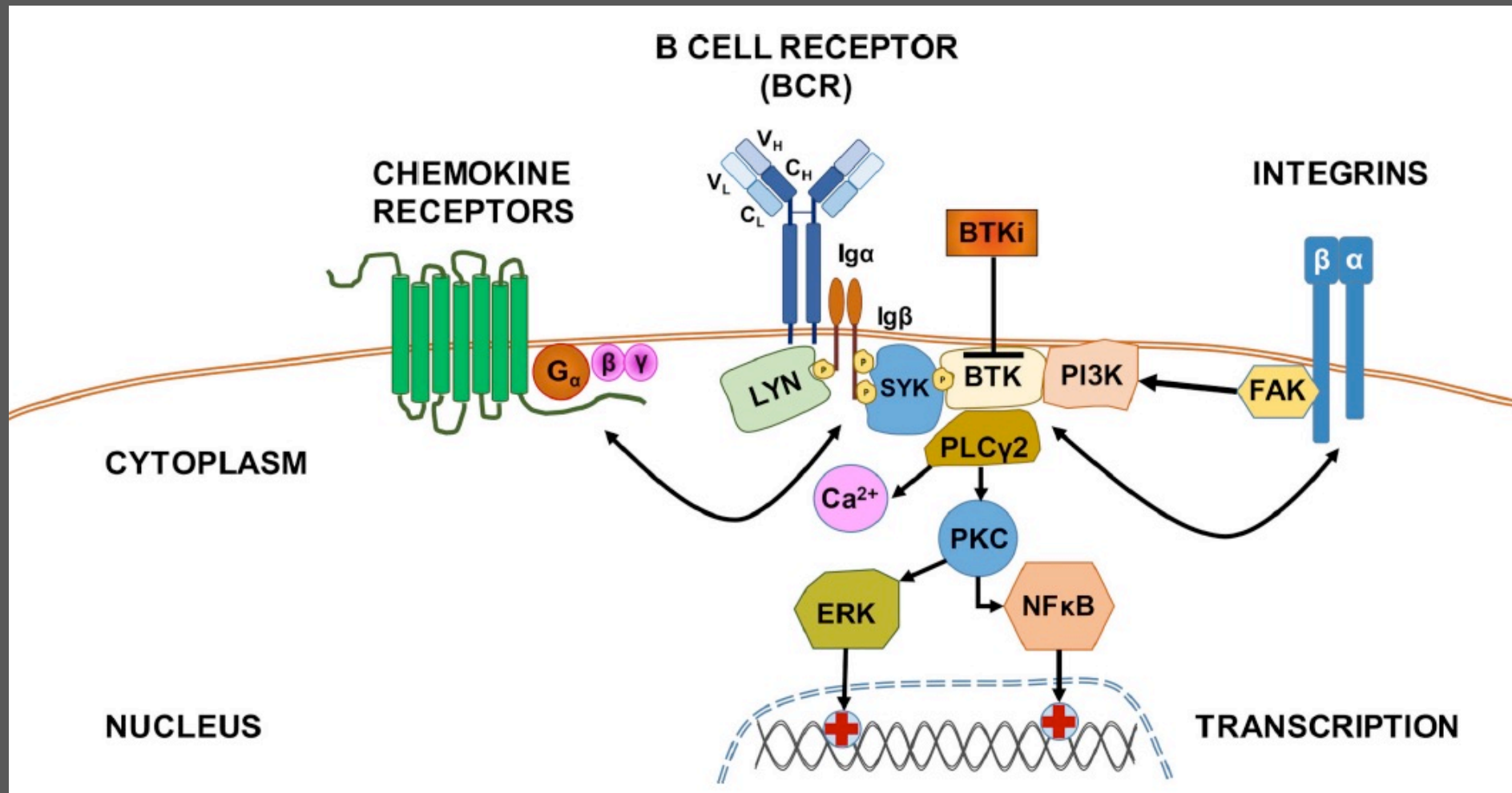




*Histopathology* 2012, 61, 930–941. DOI: 10.1111/j.1365-2559.2012.04289.x

## IRTA1 is selectively expressed in nodal and extranodal marginal zone lymphomas

Brunangelo Falini, Claudio Agostinelli,<sup>1</sup> Barbara Bigerna, Alessandra Pucciarini, Roberta Pacini, Alessia Tabarrini, Flavio Falcinelli, Milena Piccioli,<sup>1</sup> Marco Paulli,<sup>2</sup> Marcello Gambacorta,<sup>3</sup> Maurilio Ponzoni,<sup>4</sup> Enrico Tiacci, Stefano Ascani,<sup>5</sup> Maria Paola Martelli, Riccardo Dalla Favera,<sup>6</sup> Harald Stein<sup>7</sup> & Stefano A Pileri<sup>1</sup>





- V. Tabanelli
- S. Fiori
- D. Lorenzini
- A. Calleri
- F. Melle
- G. Motta
- S. Mazzara
- M.R. Sapienza
- P. Antoniotti
- S. Spagnolo
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- V. Rossi
- E Derenzini