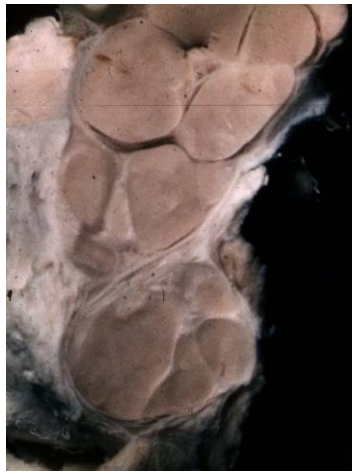
Nuove frontiere nei linfomi: il punto di vista del patologo

Hodgkin Lymphoma

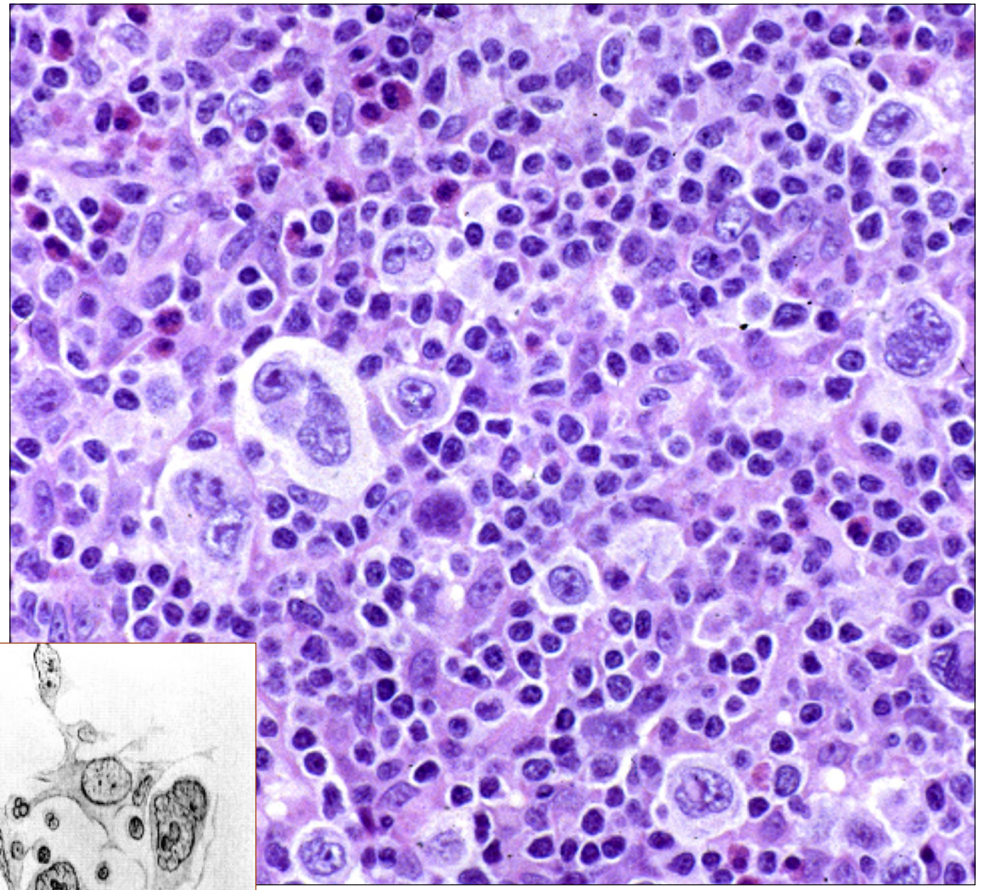
Claudio Agostinelli

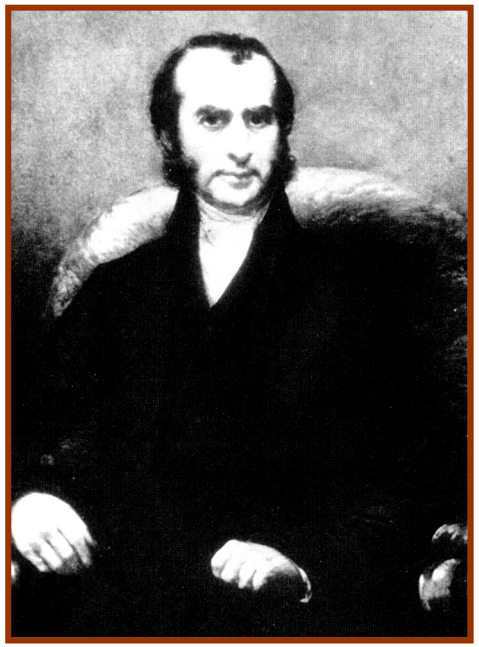
Disclosures of Claudio Agostinelli

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

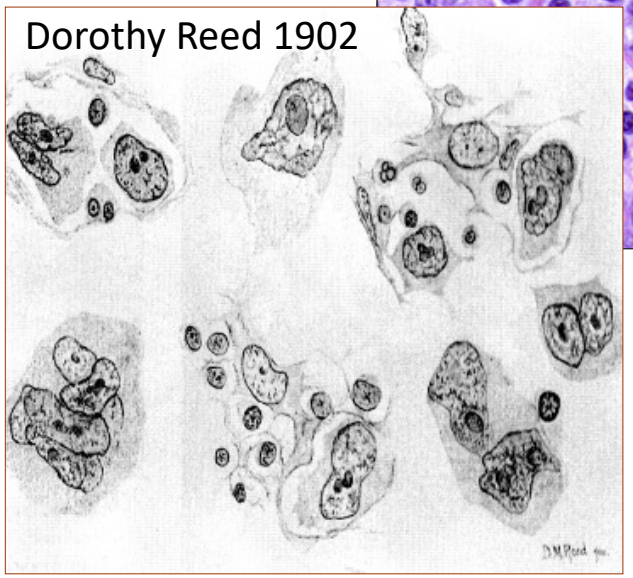


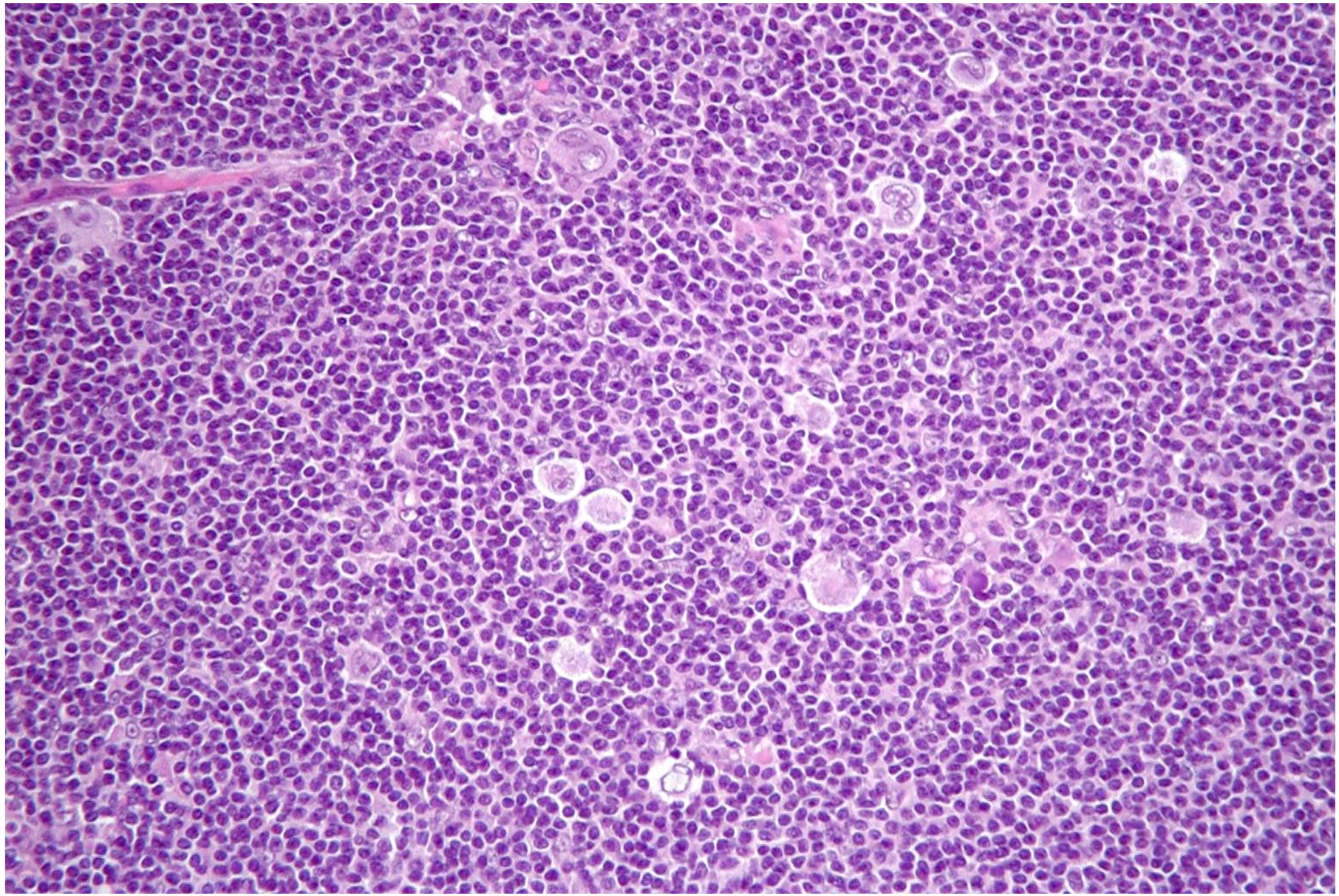
1832 Robert Lee presented at London Medico-Chirurgical Society, the “On some morbid appearances of the absorbent glands and spleen”, written by Thomas Hodgkin.



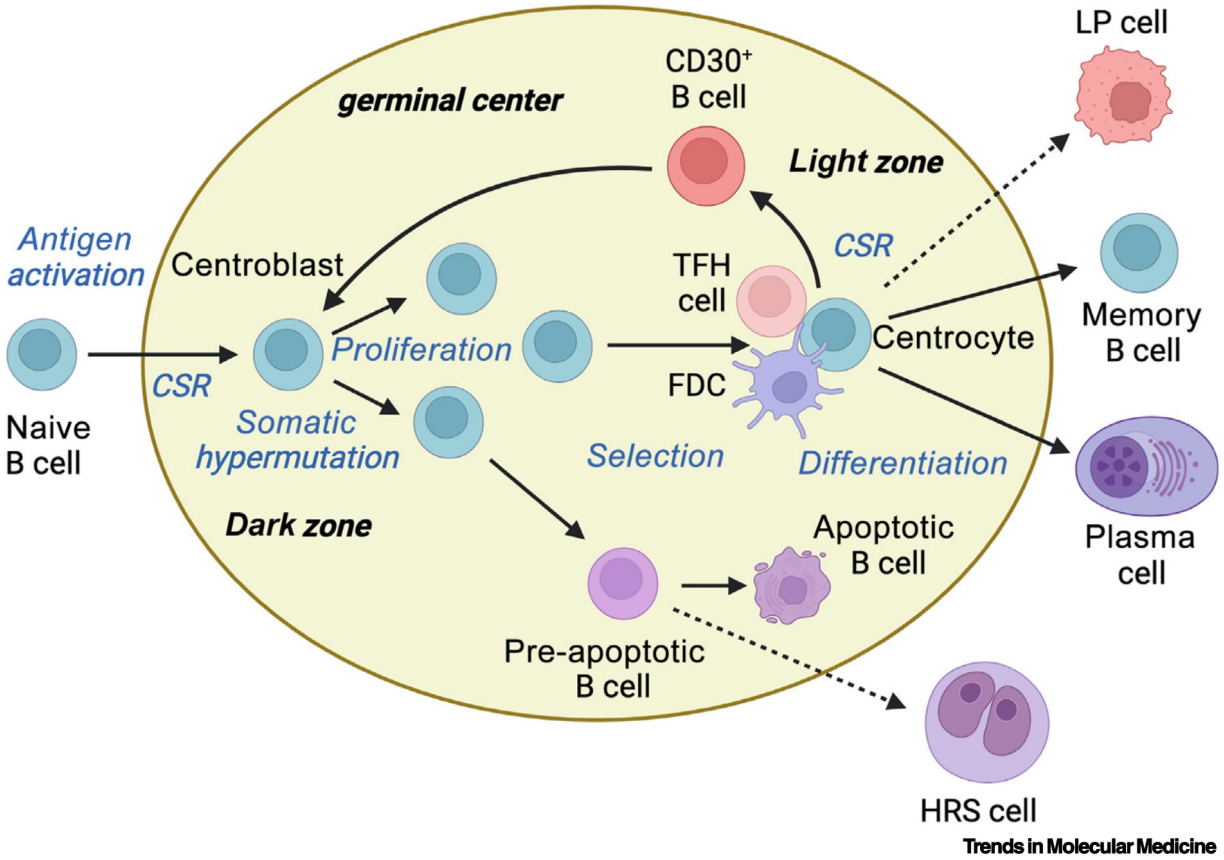


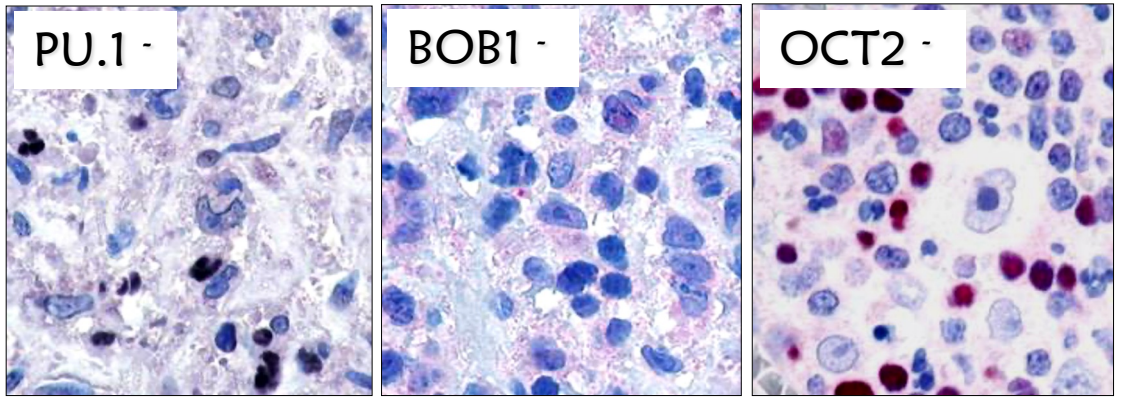
Thomas Hodgkin, Pentonville, London, August 17, 1798

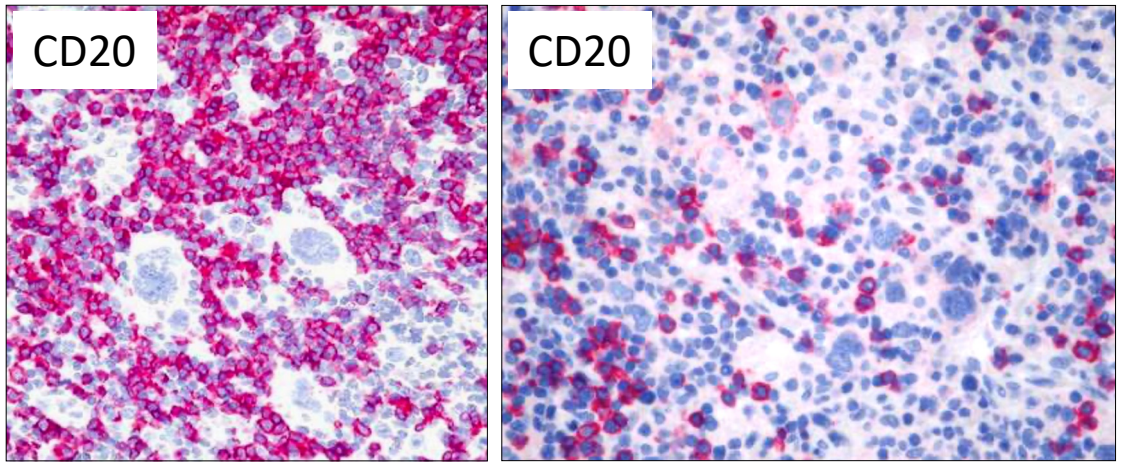




Down regolazione programma B cellulare





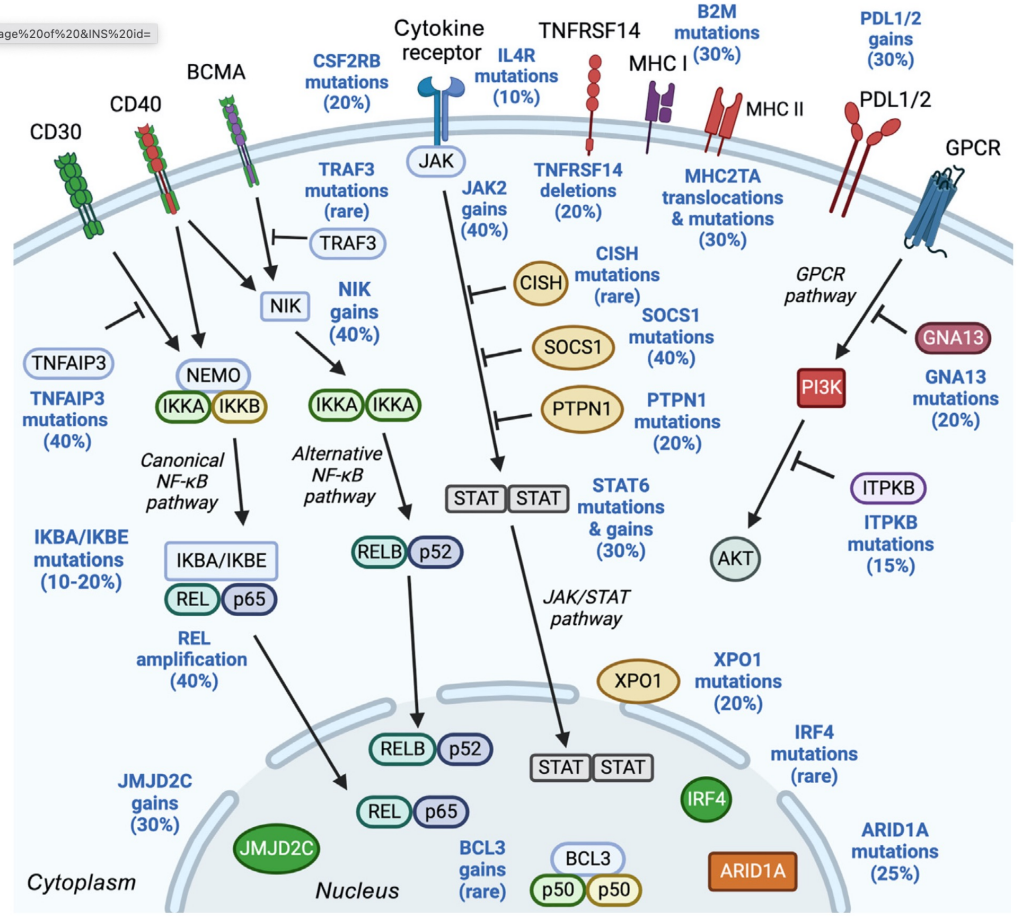


HRS e HL derivano da cellule
B mature allo stadio differenziativo
GC o post-GC

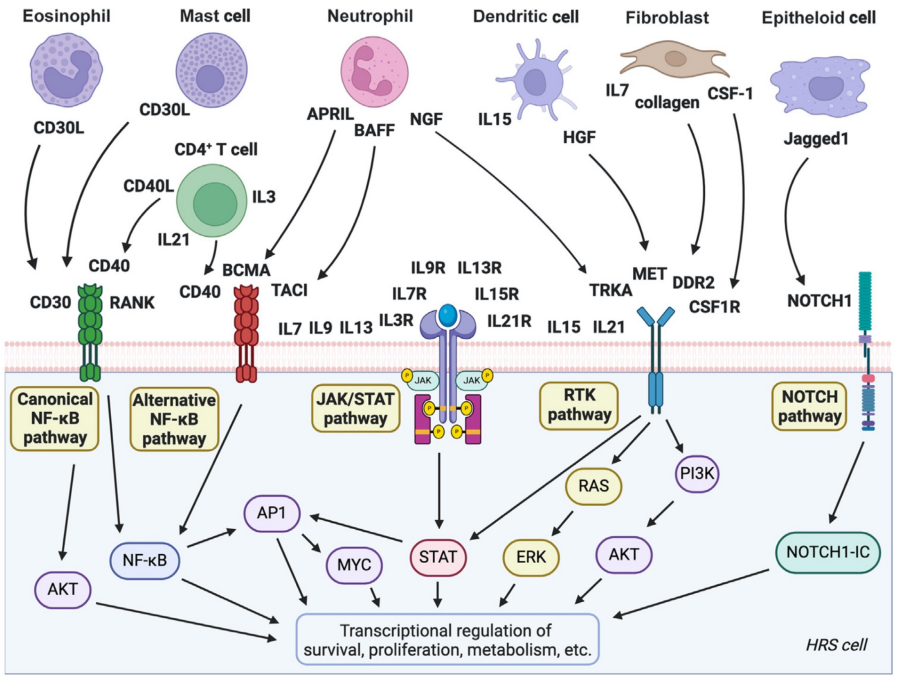
pediatric, adolescent, and young adult cases showed a higher mutation burden than adult cases.

- Group 1 was characterized by a higher somatic mutation load, more frequent mutations in members of the NF-κB, JAK/STAT, and PI3K pathways, and mainly young adult patients with the nodular sclerosis subtype
- Group 2 showed higher frequencies of copy number alterations and was enriched for EBV-positive HL

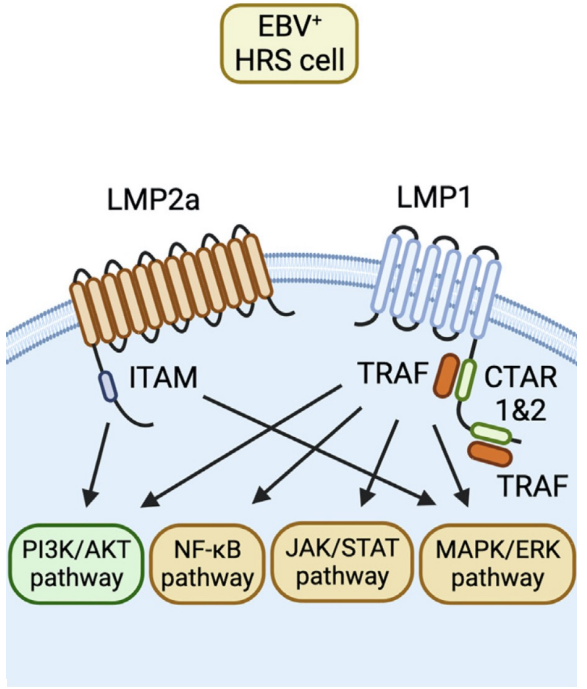
Alig, S.K. et al. (2024). Nature

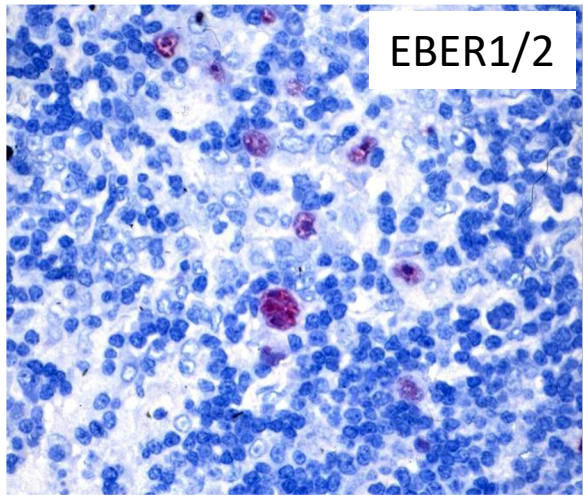


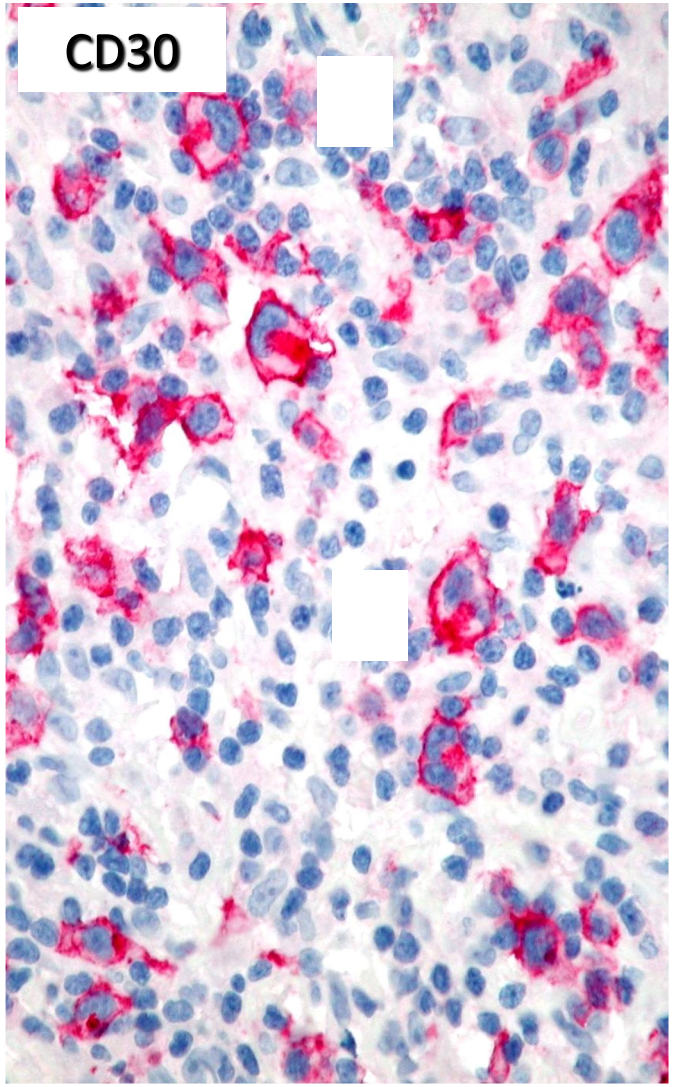
Trends in Molecular Medicine

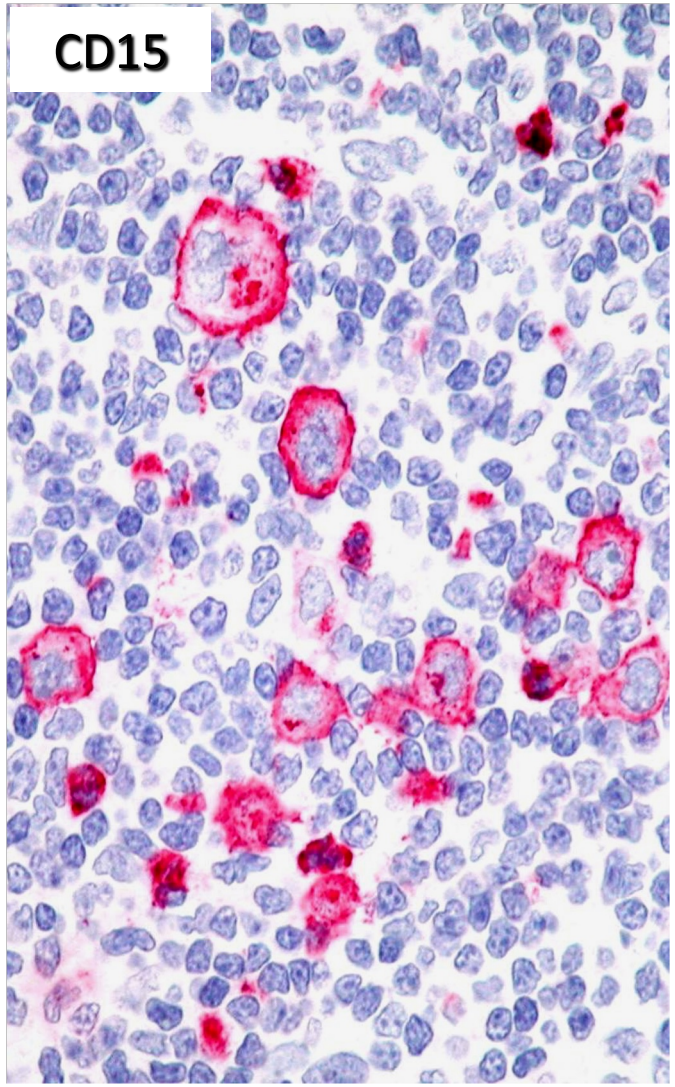


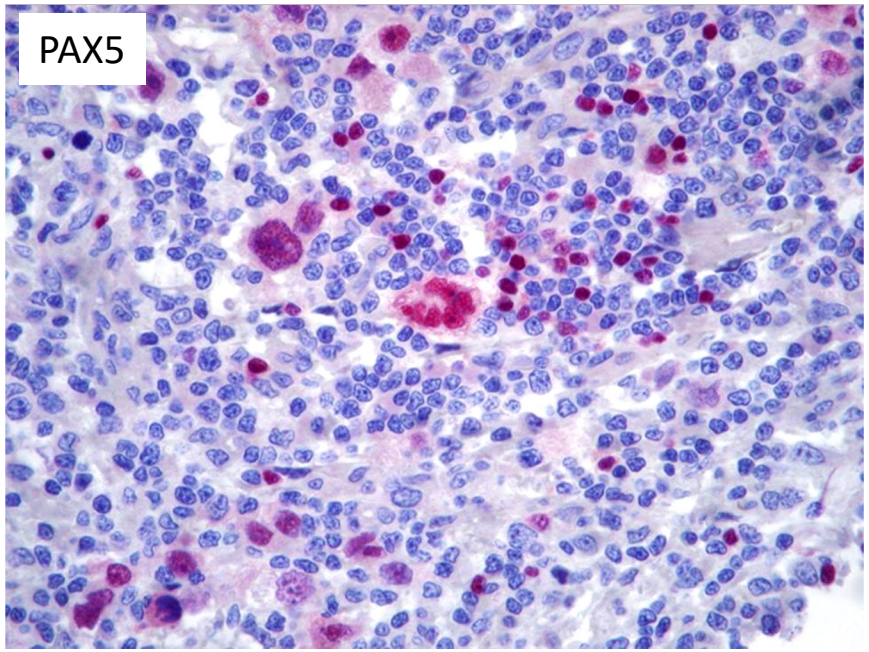
Trends in Molecular Medicine



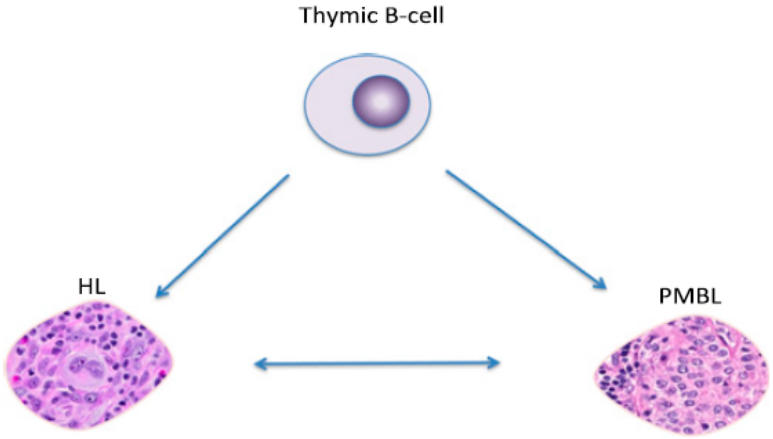


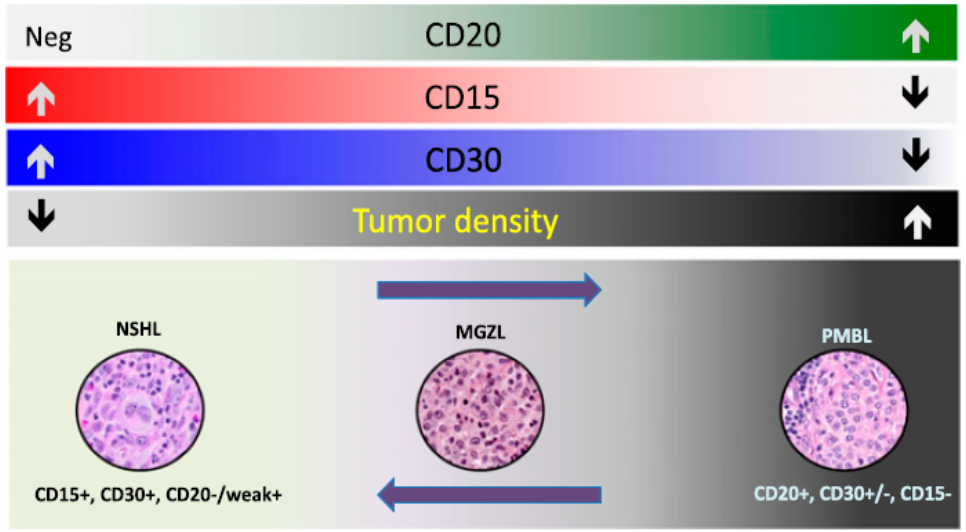


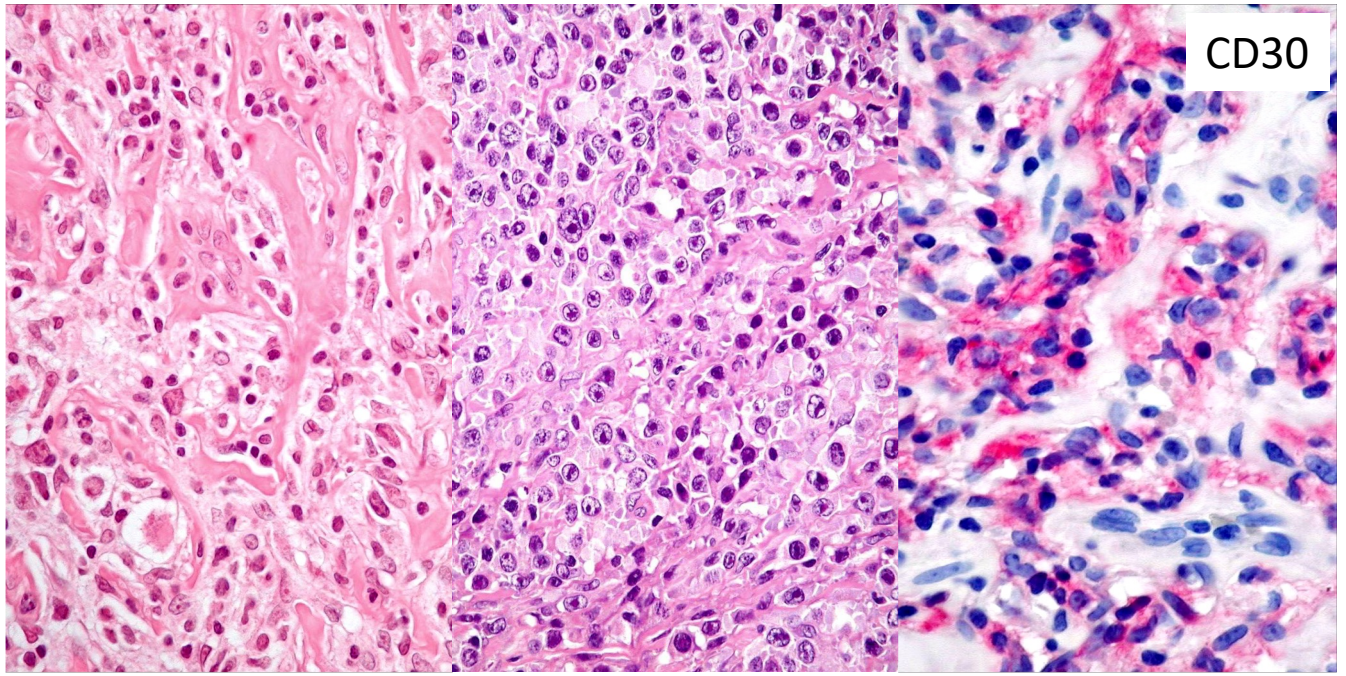




Profilo fenotipico diagnostico
CD30+
CD15+
CD20-, CD79a-, PAX5+ debole







PMBL

CD30+/CD15-
Marcatori B+ CD20/CD79a/CD19
IRF4+/BCL6+
CD23+
PDL1+
CD200+

Morphology

Evaluated histological parameters

- growth pattern: nodular, diffuse
- fibrosis: mild fibrosis without thick bands (capsular thickening included) = 1, abundant fibrosis with thick bands (capsular thickening included) = 2a, abundant fibrosis without thick bands (capsular thickening included) = 2b, no fibrosis = 0
- presence of necrosis: no, yes (if yes specify if neutrophilic)
- morphological subdivision: HL-like, PMBL-like, intermediate, composite
- amount of Hodgkin–Reed–Sternberg (HRS) cells: <10% of all neoplastic cells, >10% of all neoplastic cells
- inflammatory background: abundant = 3, moderate = 2, mild = 1, absent = 0

Immunohistochemistry

Automated immunostainers used: Ventana-Riche, Leica-Bond, Dako/Agilent

Evaluated antigens: CD45 (clone LCA, Ventana), CD30 (clone BER-H2, Ventana), CD15 (clone MMA, Ventana), CD20 (clone L26, Ventana), CD79a (clone SP18, Ventana), PAX5 (clone SP34, Ventana), OCT2 (clone MRQ-2, Cell Marque), BOB1 (clone SP92, Cell Marque), CD19 (clone LE-CD19, Dako-Agilent), IRF4/MUM1 (clone EP190, Cell Marque), Bcl6 (clone GI191E/A8, Cell Marque) and CD23 (clone SP23, Ventana).

In situ hybridization

EBER 1/2 (Epstein–Barr Virus Early Ribonucleic Acid Probe, Ventana).

Score for positive neoplastic cells

0% positive neoplastic cells: negative ('neg' in the supplementary material)
10%–25% positive cells: rare ('rare' in the supplementary material)
25%–50% positive cells: partially positive ('pp' in the supplementary material)
50%–75% positive neoplastic cells: positive ('p' in the supplementary material)
>75% positive neoplastic cells: diffuse/diffusely positive ('dp' in the supplementary material)
n.a.: not available
n.e.: not evaluable

Staining intensity: strong: 's' (in the supplementary material), moderate: 'm' (in the supplementary material), weak: 'w' (in the supplementary material), moderate to strong: 'm-s' (in the supplementary material), weak to moderate: 'w-m' (in the supplementary material)

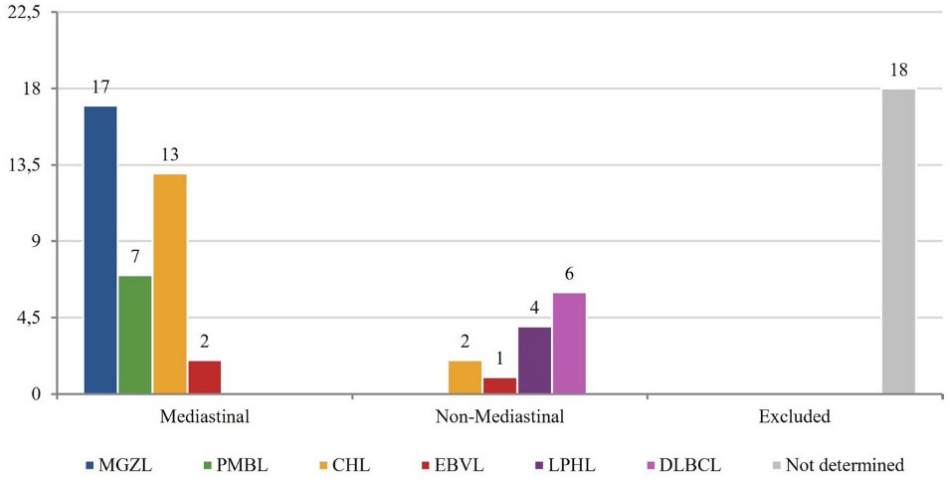
B-cell markers' combination: Upon B-cell markers availability in order, it is defined: number of B-cell markers positive in >50% neoplastic cells (include positive/p and diffusely positive/dp cases)/ number of B-cell markers positive in 25%–50% neoplastic cells (include partially positive/pp. cases)/number of B-cell markers positive in <25% neoplastic cells (include rare, negative/neg)

Virtual video shared review with Olympus DP27 camera and CellSense software

Mediastinal grey zone lymphomas: Results of the expert pathological review analysis of a case series enrolled in the multicentre BIOGZL-2020 study in Italy

Elena Sabattini[1] | Stefano Ascani[2] | Sabino Ciavarella[3] | Arianna Di Napoli[4] | Fabio Facchetti[5] | Stefano Lazzi[6] | Lorenzo Leoncini[6] | Luisa Lorenzi[5] | Marco Lucioni[7] | Giovanna Motta[1] | Nassi Luca[8] | Alice Parisi[9] | Marco Paulli[7] | Stefano Pileri[10] | Maurilio Ponzoni[11] | Claudio Tripodo[12] | Simona Righi[13] | Claudio Agostinelli[1,13]

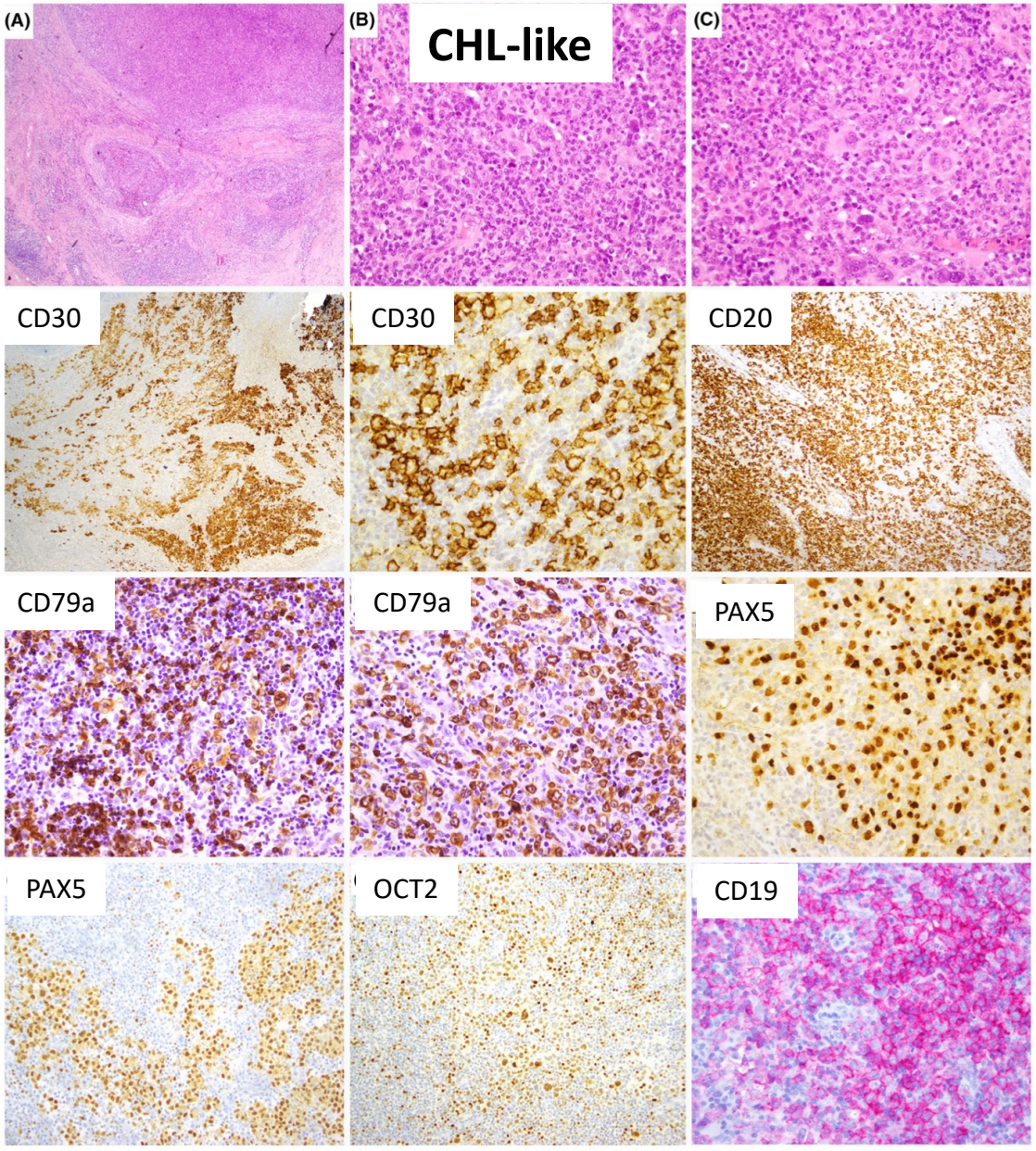
- 70 cases (14 italian centres)
- assessing the degree of reproducibility,
- providing general guidelines and/or recommendations for daily practice

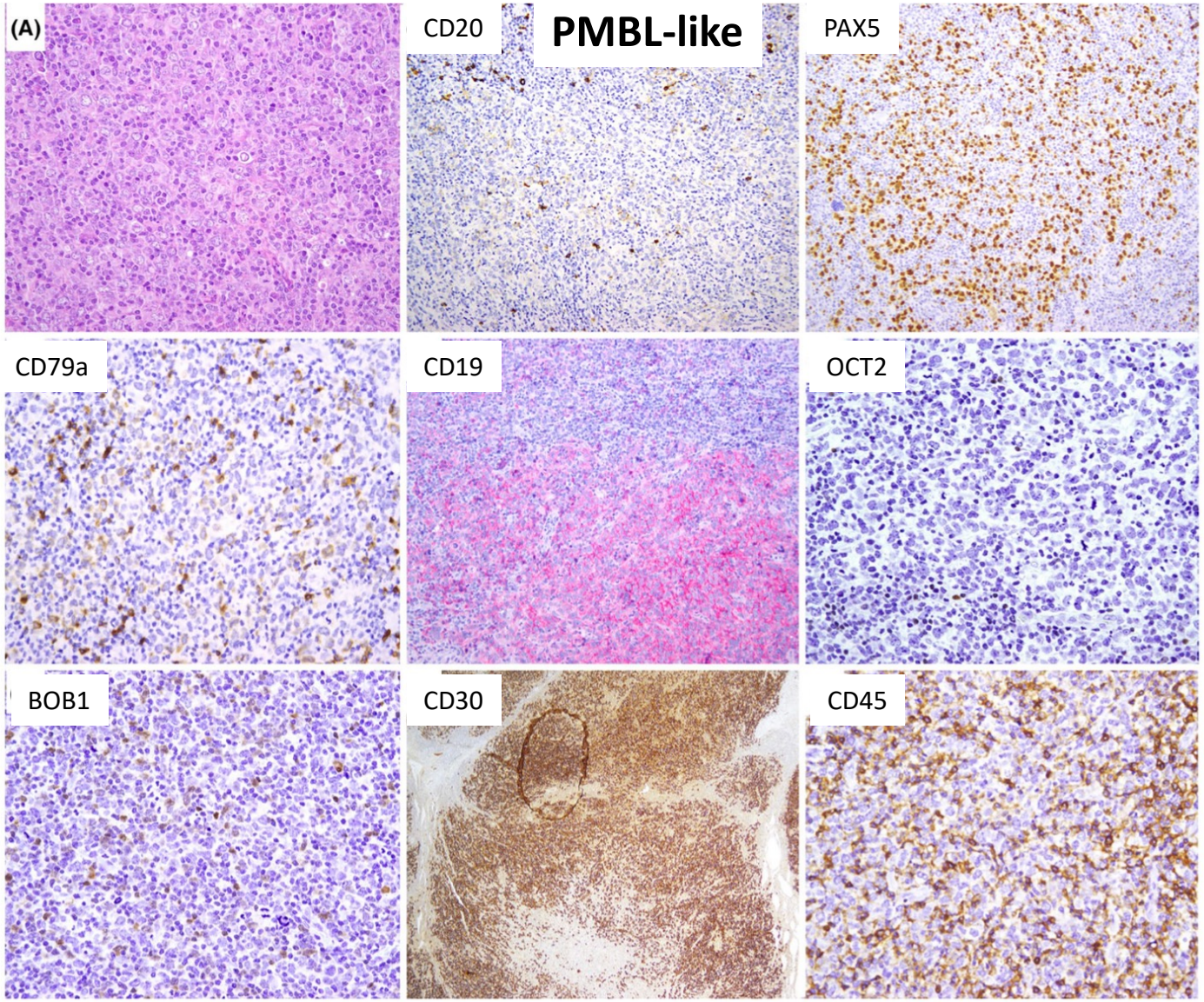


BJH 2026

- average age was 35.23years (range 17–51),
- 12 (70.5%) were males;
- all had mediastinal masses (bulky in 14)
- biopsy site was mediastinum in four cases, cervical or supraclavicular LN.

17 (24.28%) cases confirmed as MGZL (mediastinal/EBV negative)	
MGZL-CHL (cases n. 1–4)	4 (23.52%)
MGZL-PMBL (cases n. 5–13*)	9 (52.94%)
Intermediate# (cases n. 14–17)	4 (17.64%)
35 (50%) cases reclassified	
Mediastinal/EBV negative (20 cases; 57.14%)	
PMBL (cases n. 18–24)	7
CHL (cases n. 25–37*)	13
Non-mediastinal-EBV negative (12 cases; 34.28%)	
DLBCL (cases n. 38–42)	5
B-cell lymphoma related to LPHL (cases n. 43–46**)	4
CHL (cases n. 47–48)	2
LBCL with GZL-like features in Human Immunodeficiency Virus (HIV) (case n.49)	1
EBV positive (3 cases; 8.5%)	
Mediastinal/LBCL (cases n. 50–51)	2
Non-mediastinal/LBCL (case n. 52)	1
18 (25.71%) cases excluded from evaluation	
Suboptimal/poor material (cases n. 53–67)	15
Only needle biopsies available (cases n. 68–70)	3





Convegno Regionale

SIE LE NUOVE FRONTIERE NELLA TERAPIA DEL LINFOMA: INNOVAZIONE E FUTURO

DELEGAZIONE CAMPANIA

30 Marzo 2026

Napoli, *Centro Congressi Federico II*

Società Italiana di Ematologia

Conclusion:

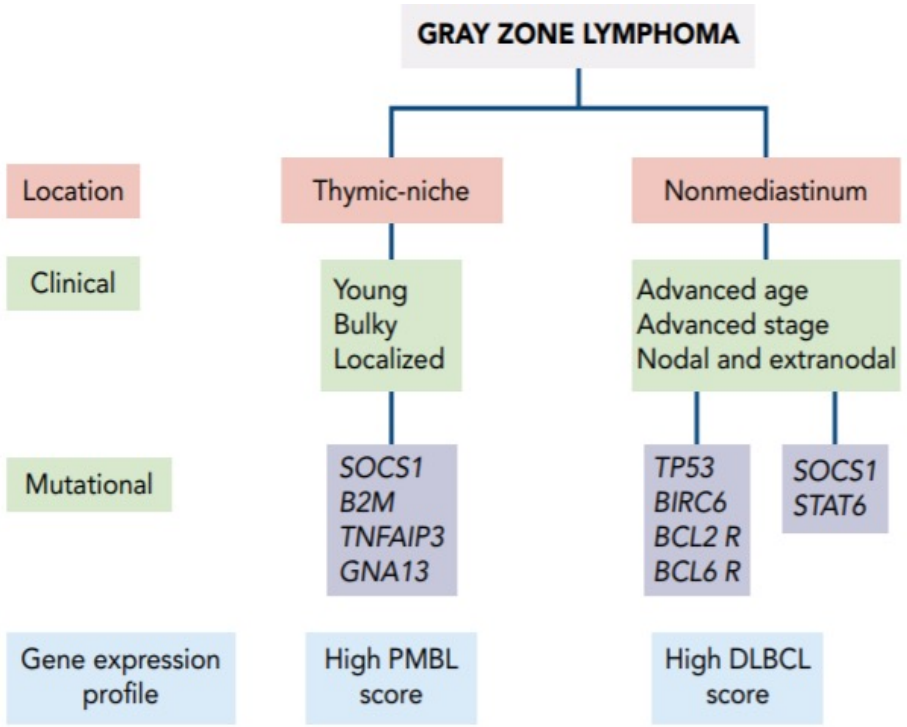
- MGZL shows high variability and heterogeneity in the combination of morphology and phenotype (number of positive B- cell markers, staining intensity, percentage of positive neoplastic cells): all these features must be considered collectively, case by case,

- Apply wide set of B-cell molecules trying to adhere to the recent classifications criteria, being aware that not all cases may easily be included.

- Caution is recommended in otherwise CHL expressing only, yet strongly, CD20 or partially expressing more B antigens, as well as in syncytial/sheeting DLBCL-like lymphomas with an otherwise CHL phenotype.

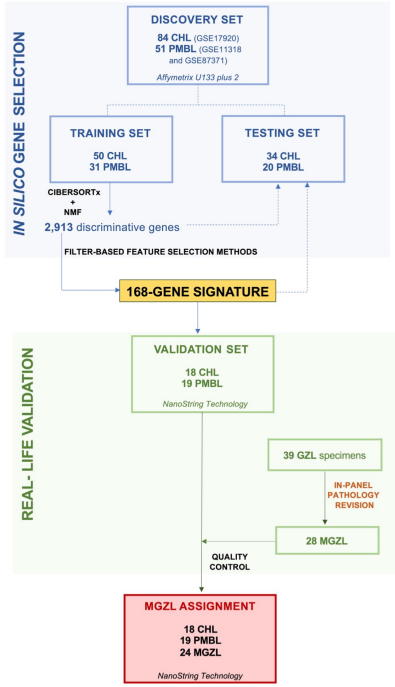
- A second opinion to corroborate and/or share the diagnosis may be necessary and/or desirable.

- Availability of adequate tissue as regards both quantity and quality is the *conditio* sine qua non for a histopathological diagnosis of MGZL: the recommendation is to refrain to make a definitive diagnosis of MGZL in small samples, requiring additional tissue and in case it is still not sufficient or not interpretable or not feasible, clearly state to resample if the clinical response is not as expected.

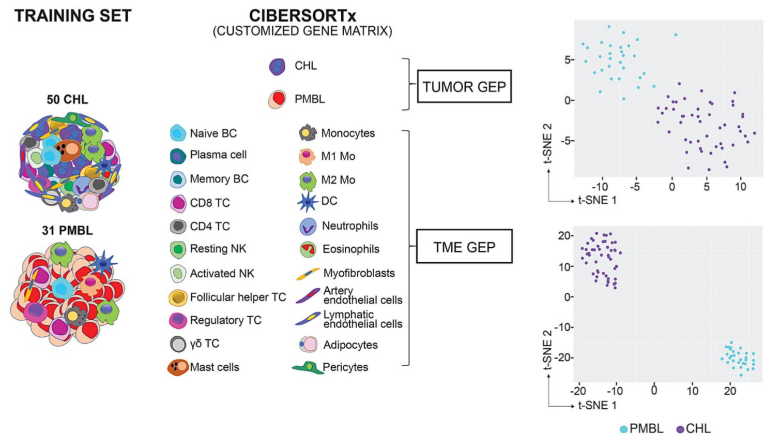


Sarkozy C *et al* Blood Advances, 2020; Campo & Jaffe Blood 2021

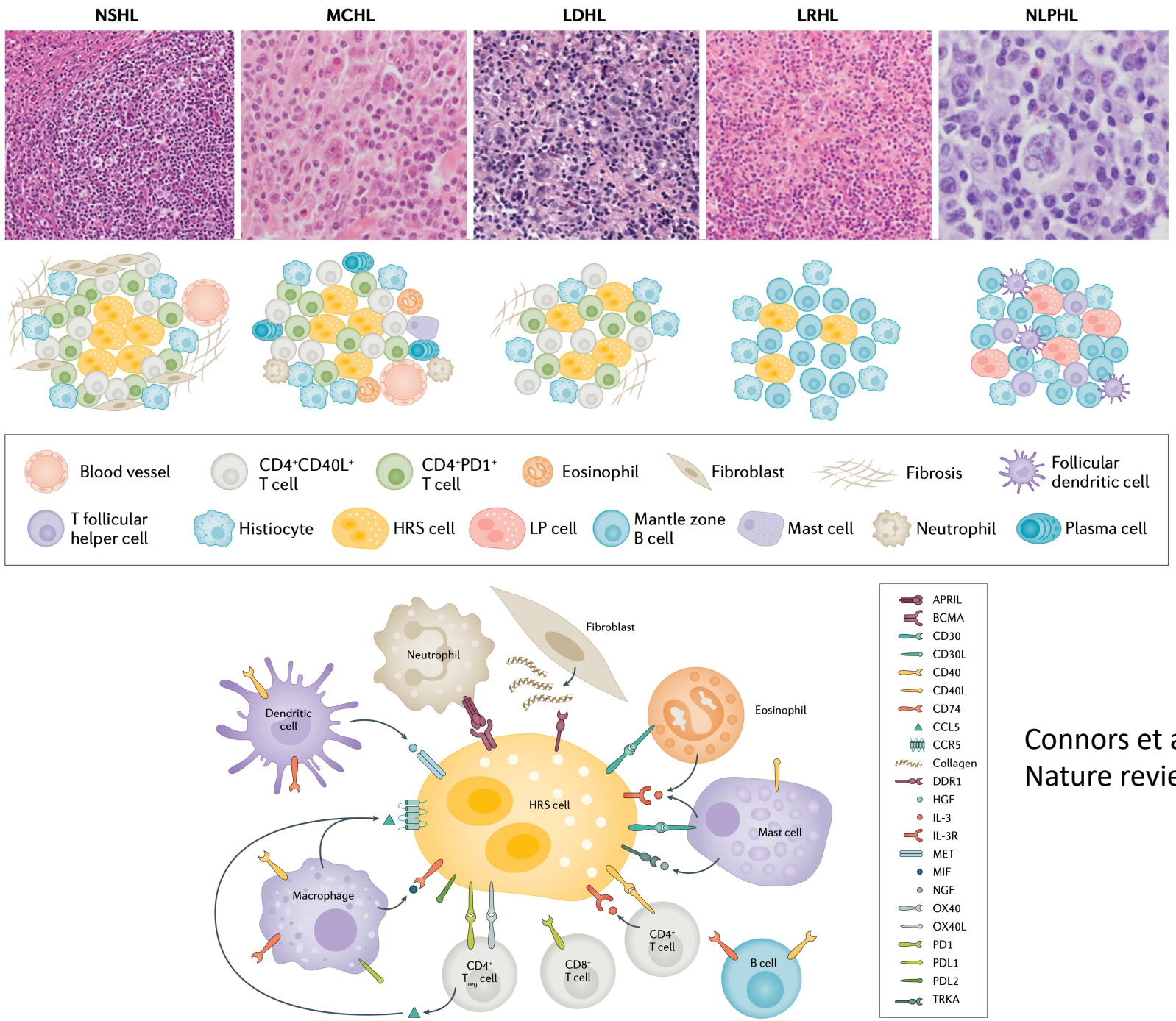
A targeted gene signature stratifying mediastinal gray zone lymphoma into classical Hodgkin lymphoma-like or primary mediastinal B-cell lymphoma-like subtypes



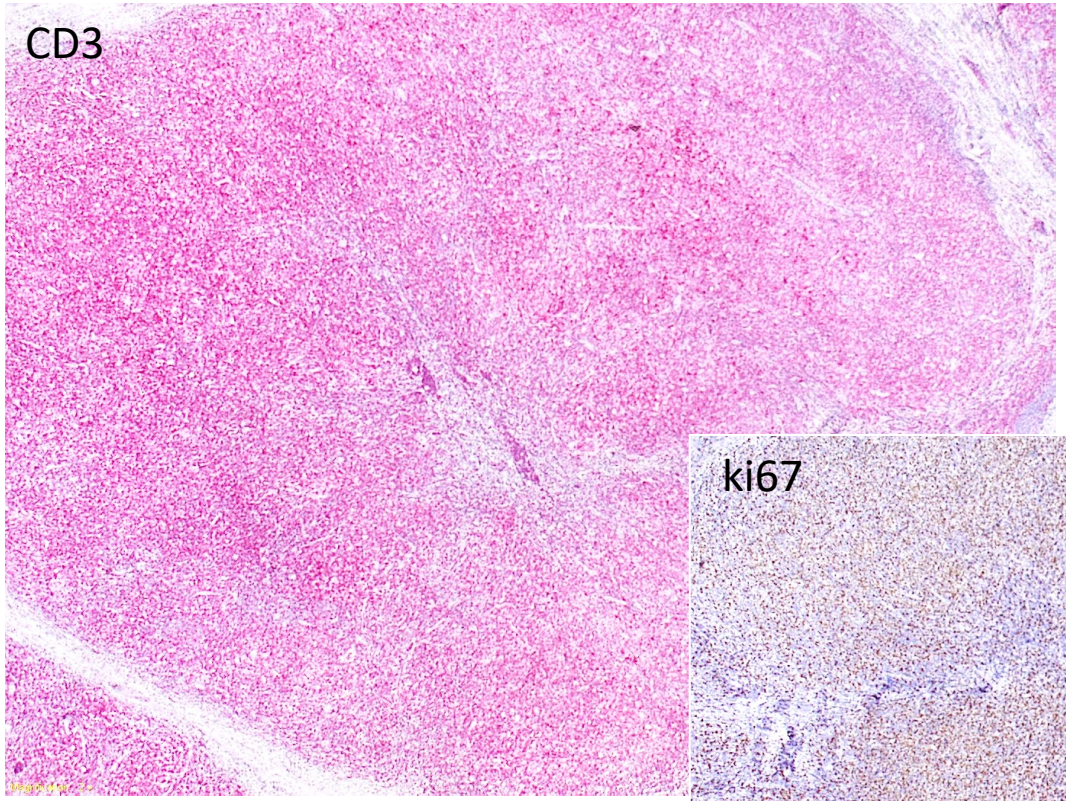
Gargano et al Haematologica 2024

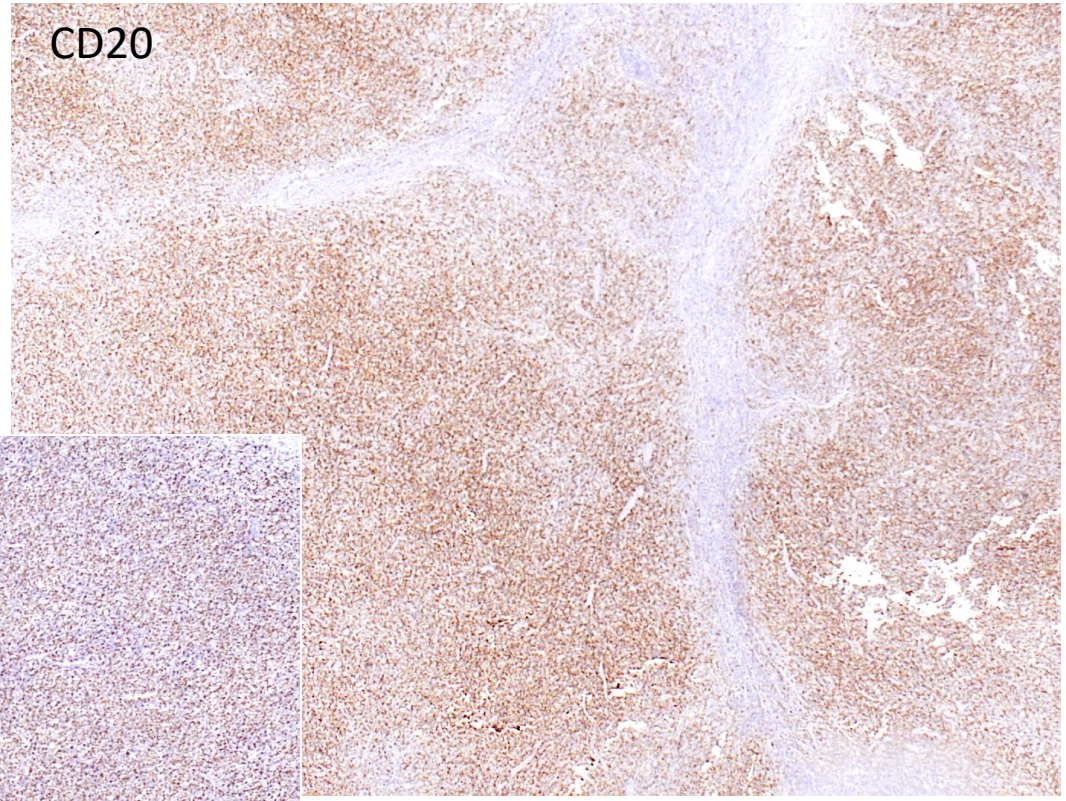


«build a combined histopathological/transcriptomic model of MGZL stratification and, ultimately, to prompt its translation into the clinical setting in order to optimize the treatment»



Connors et al
Nature reviews Disease Primers (2020)


CD3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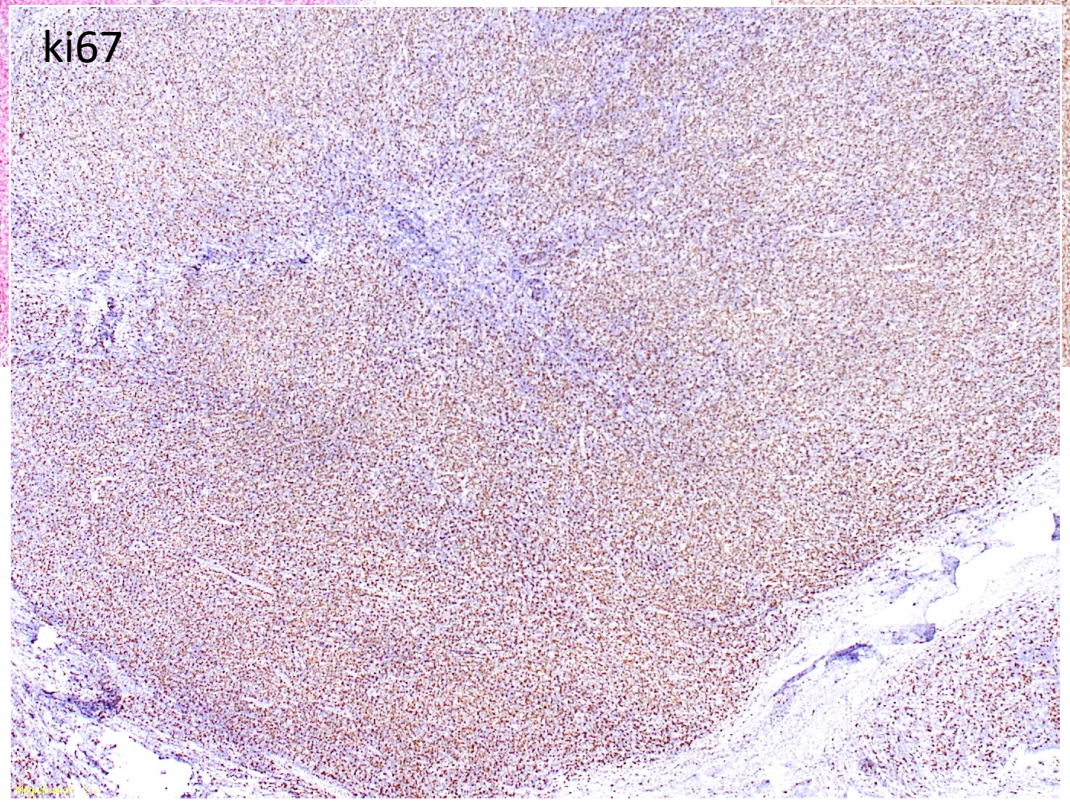
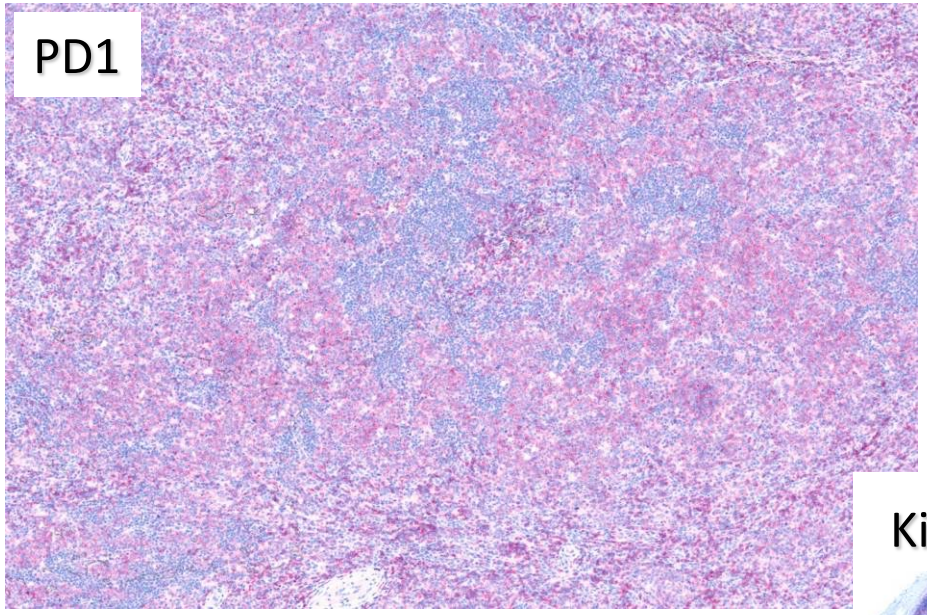

ki67

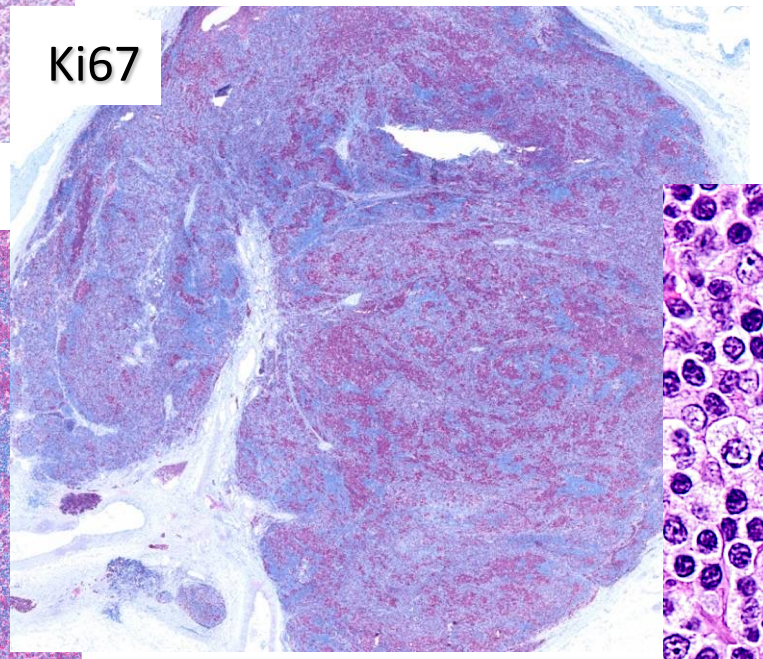


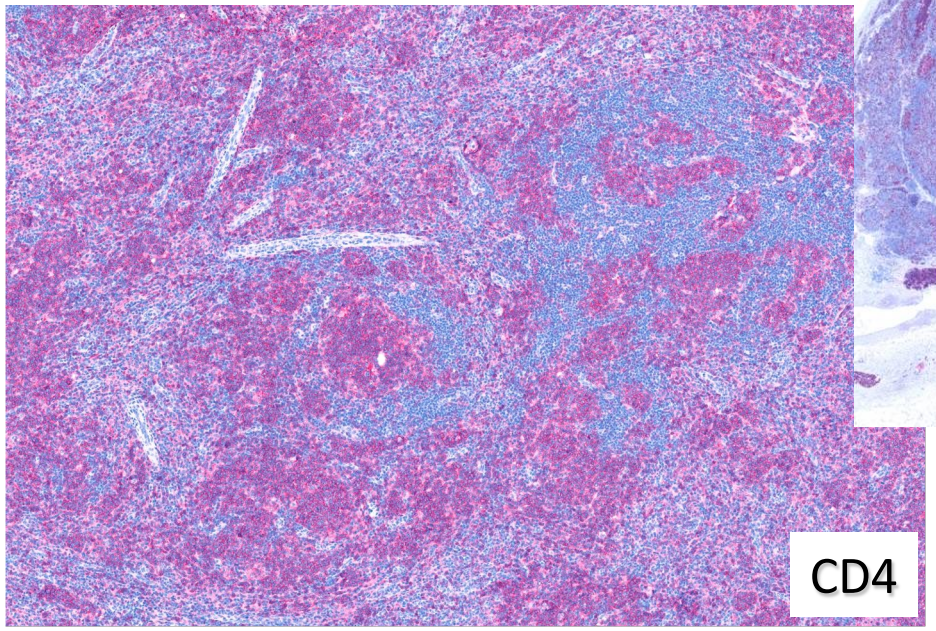
Peripheral T-cell lymphoma, NOS

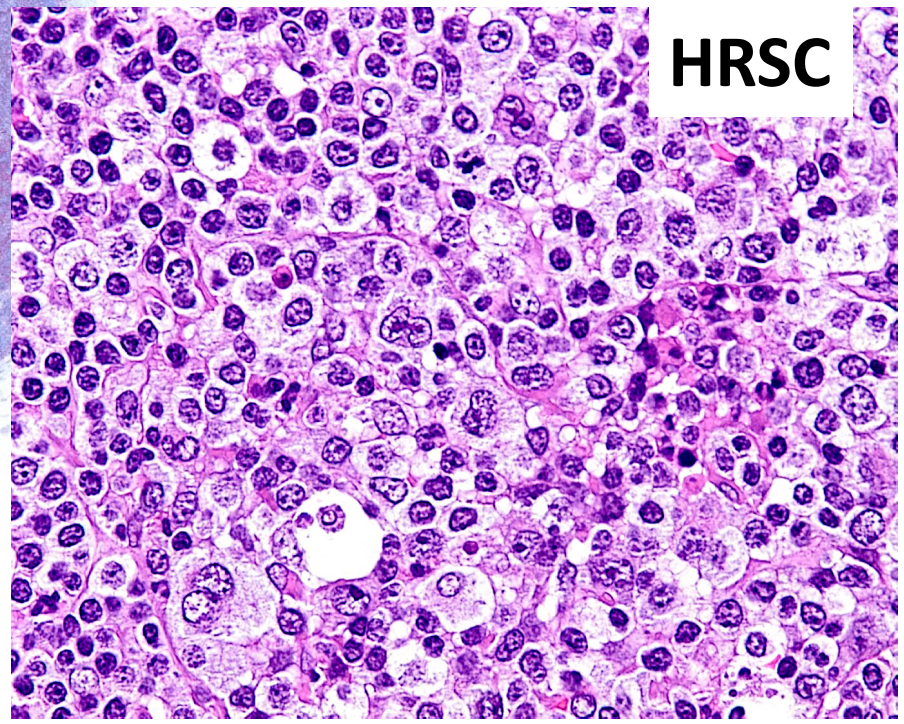
Angioimmunoblastic T-cell lymphoma

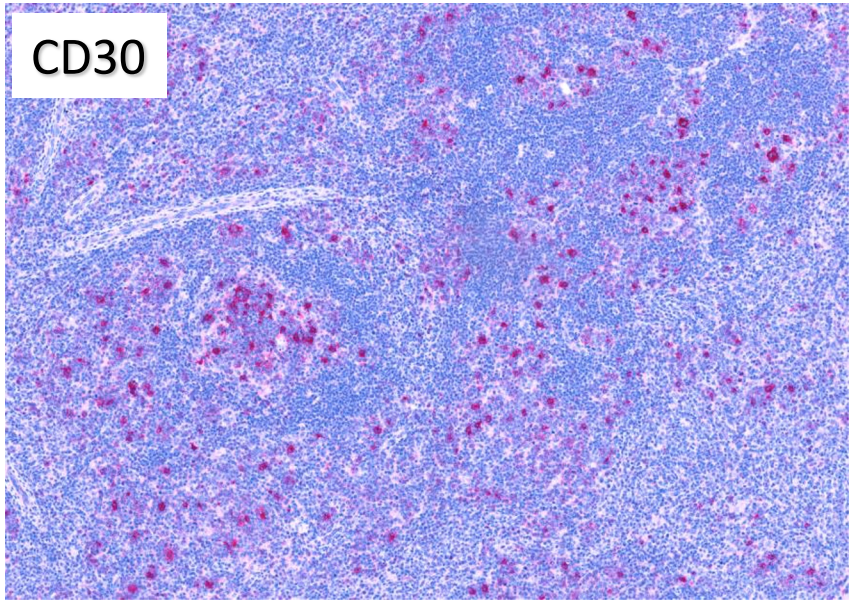
*Follicular T-cell lymphoma**

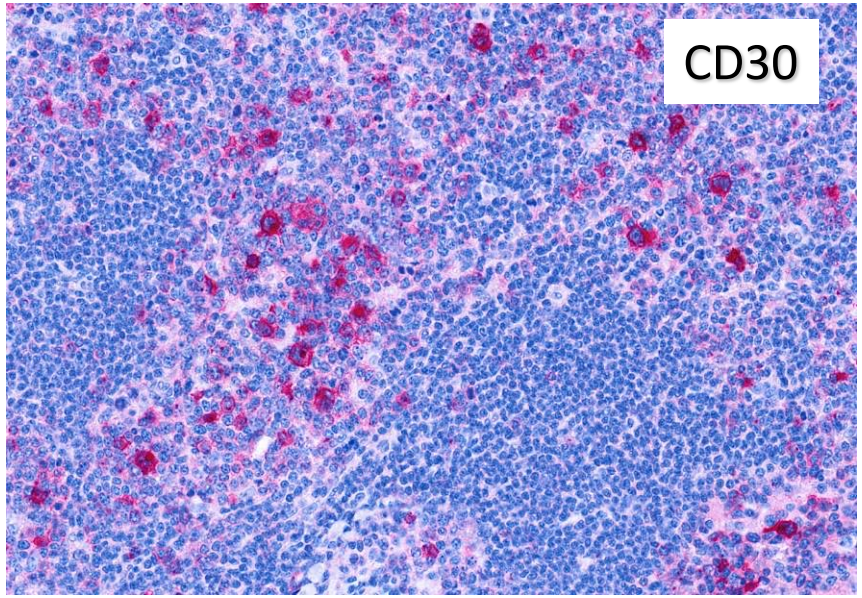
*Nodal peripheral T-cell lymphoma with TFH phenotype**

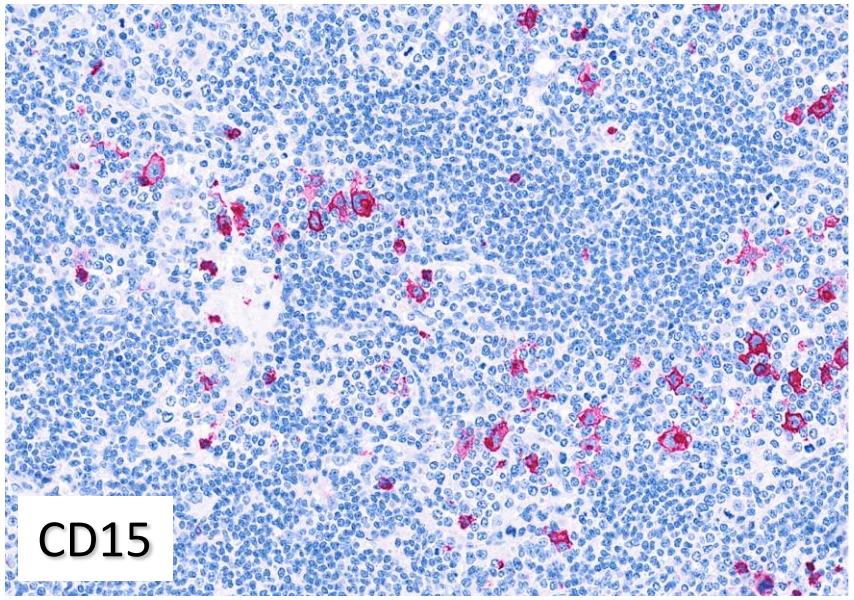







CD30


CD30


CD15

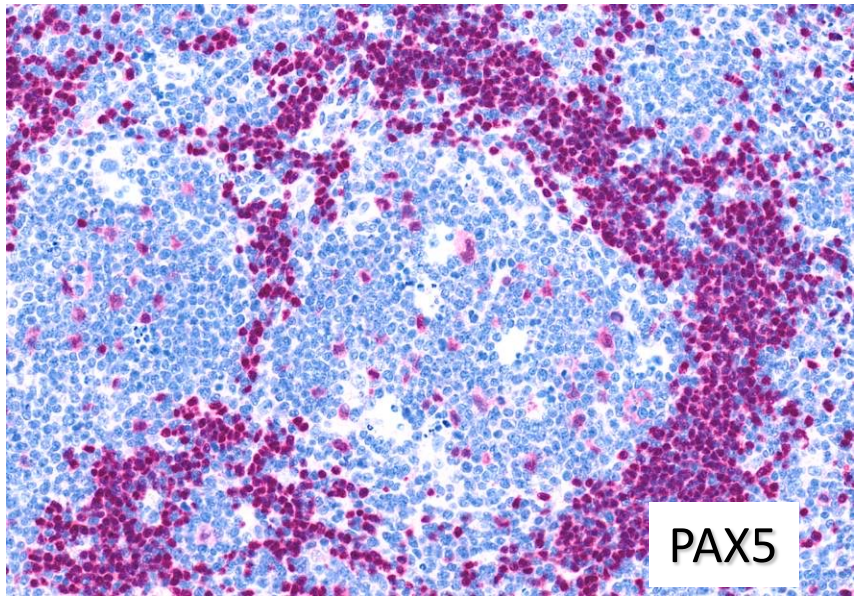

PAX5

TABLE 2. Comparison of Morphologic, Phenotypic, and Molecular Features Between TFHL and CHL

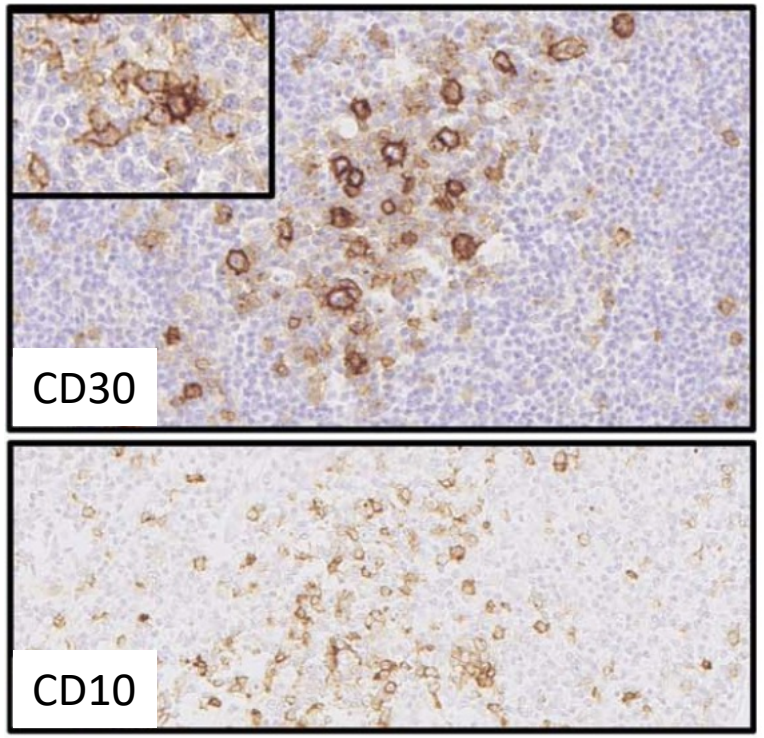
	TFHL (n = 15)	CHL (n = 12)	*P*
Cytologic features			
T-cell atypia			0.020
None/minimal	9/15	12/12	—
Moderate/marked	6/15	0/12	—
Clear cytoplasm (T cells)	8/15	3/12	0.239
HRS (-like) cells			0.002
Rare/few	12/15	2/12	—
Moderate/abundant	3/15	10/12	—
Architectural features			
Sinus sign	8/15	1/7	0.165
Parenchymal fibrosis	6/15	8/12	0.252
Capsular fibrosis	12/15	5/7	1.000
HEV proliferation			0.005
Minimal	4/15	3/12	—
Moderate/marked	10/15	1/12	—
FDC expansion	7/15	0/12	0.008
T cells IHC			
CD7 loss	4/15	0/12	0.106
CD10+	13/15	0/12	< 0.001
CXCL13+	14/14	6/9	0.047
PD1 strongly*+	13/15	2/12	< 0.001
ICOS+	15/15	12/12	—
BCL6+	9/14	3/10	0.214
CD30+	12/15	0/12	< 0.001
HRS (-like) cells IHC			
CD20+	12/15	2/12	0.002
PAX5 strongly+	10/15	4/12	0.128
CD79a+	13/14	2/11	< 0.001
CD19+	8/13	1/10	0.029
CD22+	1/13	0/10	1.000
BOB1+	5/14	0/10	0.053
OCT2+	11/14	3/10	0.035
CD30+	15/15	12/12	—
CD15+	9/15	10/12	0.236
EBER and/or LMP1 +	13/15	6/12	0.087
Clonality studies			
B-cell clone	3/13	5/12	0.376
T-cell clone	9/12	0/12	< 0.001
RHOA G17V PCR	8/10	0/6	0.007
NGS			
TET2 mut	14/14	3/12	< 0.001
1 mutation	6/14	1/12	—
2 mutations	8/14	2/12	—
DNMT3A	4/14	0/12	0.100
RHOA	13/14	0/12	< 0.001
IDH2	1/14	0/12	1.000

Follicular Helper T-cell Lymphoma With Hodgkin/Reed-Sternberg–Like Cells Versus Classic Hodgkin Lymphoma

A Comparative Study

Sara Petronilho, MD,†‡ Elsa Poullot, MD,*§‖ Axel Andre, MD,§‖¶ Cyrielle Robe, MD,*§‖ Sako Nouhoum, PhD,*§‖ Virginie Fataccioli, MD,*§ José Miguel Quintela, MD,# Alexis Claudel, MD,§‖¶ Josette Brière, MD,* Emmanuele Lechapt, MD, PhD,*§‖ François Lemonnier, MD, PhD,§‖** Rui Henrique, MD, PhD,††† Laurence de Leval, MD, PhD,‡‡ and Philippe Gaulard, MD*§‖*

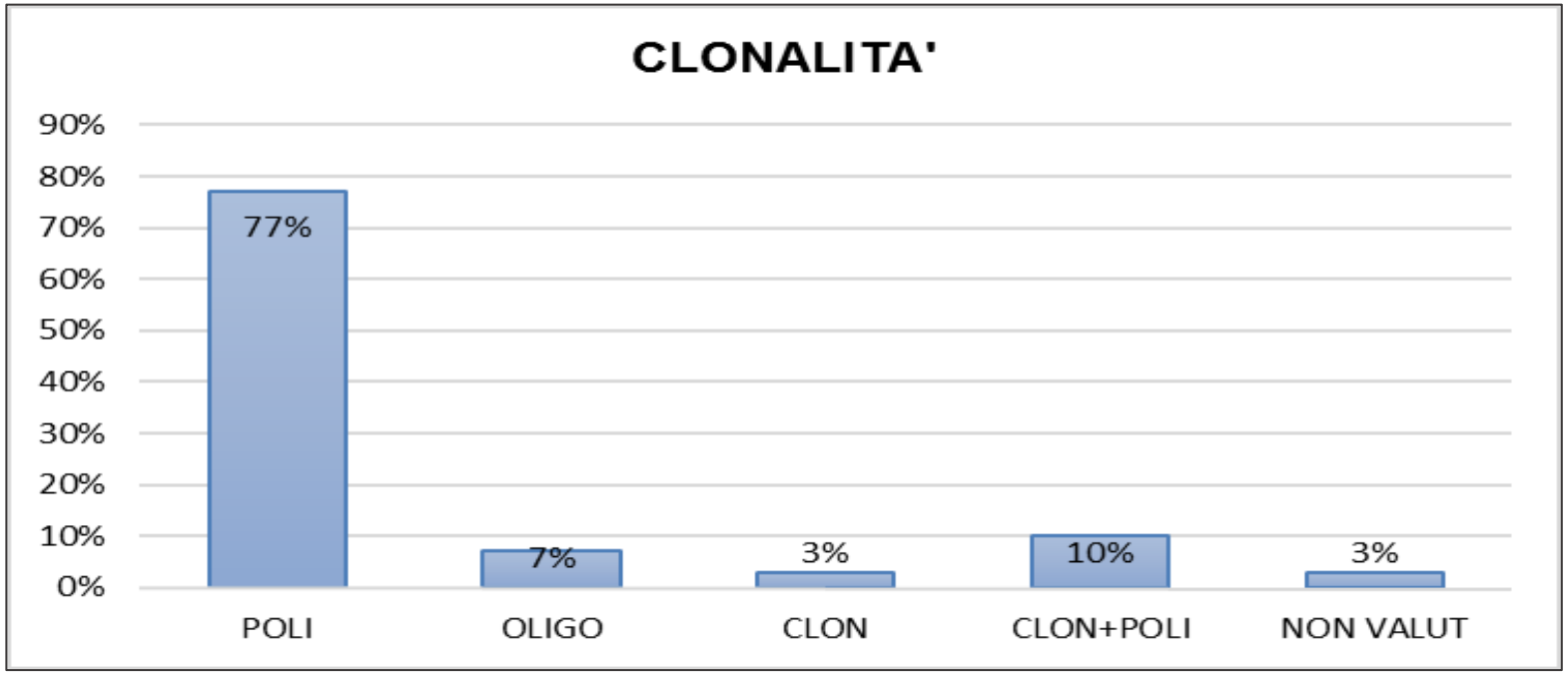
- The most useful TFH marker was CD10 (positive in 86% TFHL and no CHL). Twelve/15 TFHL contained CD30+ neoplastic TFH cells, whereas CD30 expression was mostly restricted to HRS cells in CHL.
- monoclonal TR rearrangements in 75% of TFHL and no CHL; monoclonal IG rearrangements in 23% of TFHL and 42% of CHL.
- All TFHL had TET2 mutations; 13/14 presented RHOA mutations, 3 accompanied by DNMT3A and 1 DNMT3A+IDH2 mutations.
- phenotypically abnormal circulating T-cell population in the peripheral blood by flow cytometry may bea clue to the identification of TFHL mimicking CHL

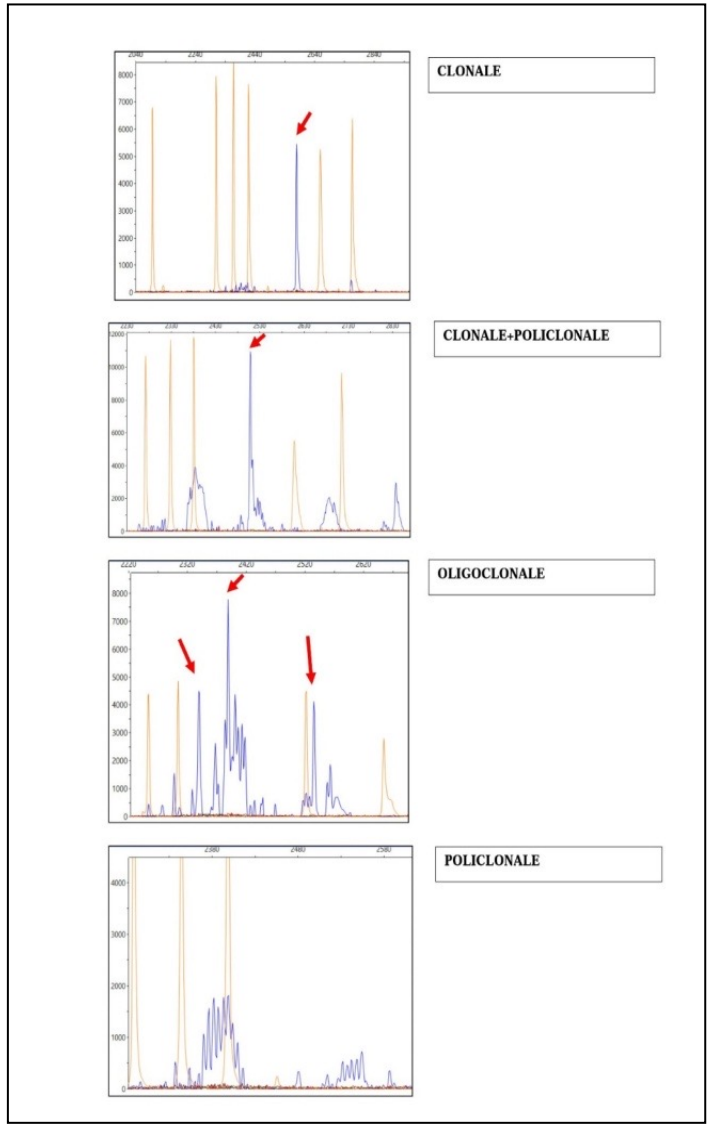


no single pathologic criterion distinguishes TFHL and CHL, an integrative approach ideally comprising molecular in- vestigations is fundamental.

- Atipia linfociti T
- Linfociti T: cellule chiare
- Fenotipo aberrante
- Fenotipo TFH
- Ki67 alto
- ***TRG riarrangiato***

Saggio clonalità TRG in 70 cHL





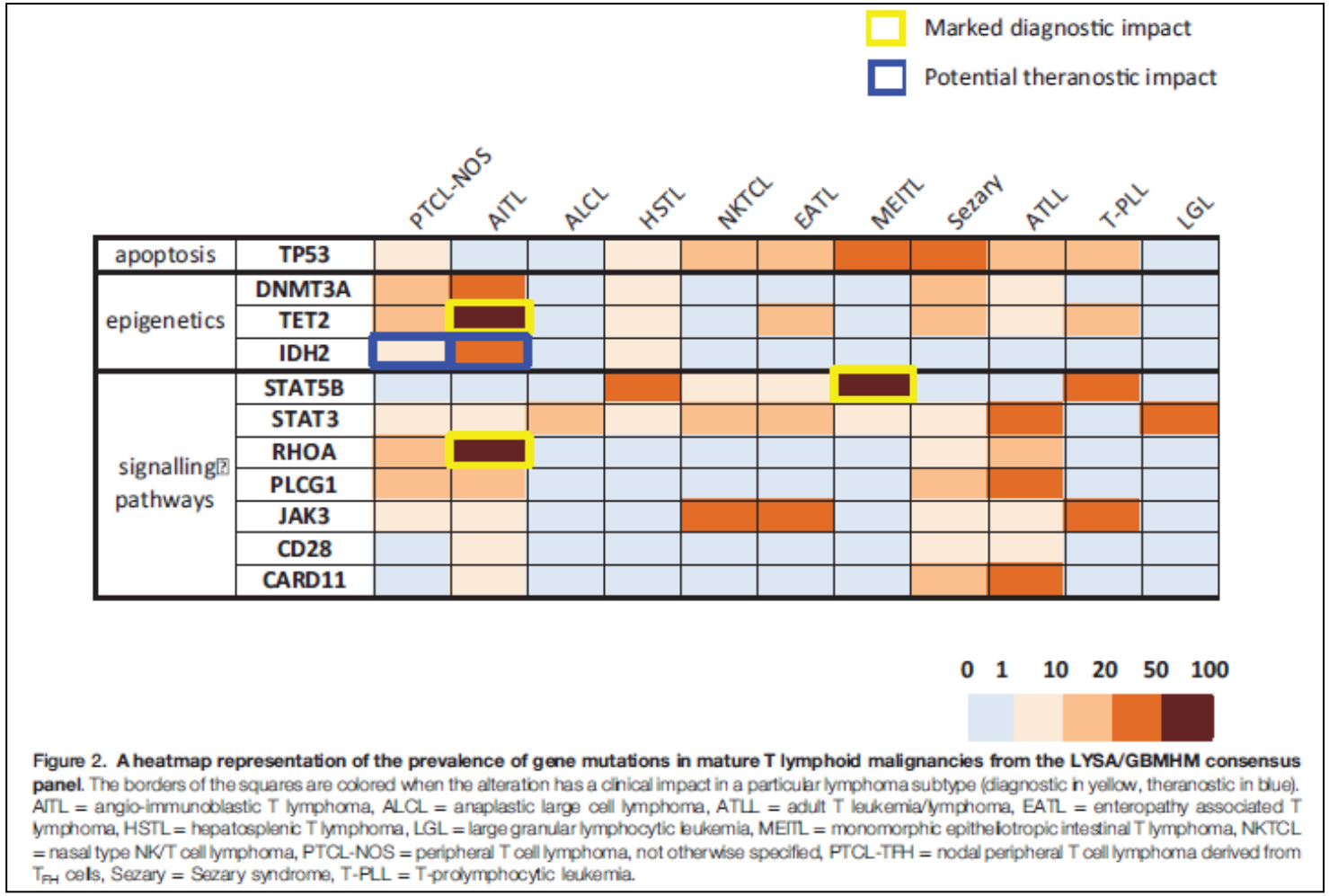


Figure 2. A heatmap representation of the prevalence of gene mutations in mature T lymphoid malignancies from the LYSA/GBMHM consensus panel. The borders of the squares are colored when the alteration has a clinical impact in a particular lymphoma subtype (diagnostic in yellow, theranostic in blue). AITL = angio-immunoblastic T lymphoma, ALCL = anaplastic large cell lymphoma, ATLL = adult T leukemia/lymphoma, EATL = enteropathy associated T lymphoma, HSTL = hepatosplenic T lymphoma, LGL = large granular lymphocytic leukemia, MEITL = monomorphic epitheliotropic intestinal T lymphoma, NKTCL = nasal type NK/T cell lymphoma, PTCL-NOS = peripheral T cell lymphoma, not otherwise specified, PTCL-TFH = nodal peripheral T cell lymphoma derived from T_{FH} cells, Sezary = Sezary syndrome, T-PLL = T-prolymphocytic leukemia.

Pannello NGS

DNMT3A
TET2
$IDH2^{R172}$
$RHOA^{G17V}$

!!!!! TET2 and DNMT3A mutations are not specific to TFHL and may reflect clonal hematopoiesis.!!!!!

Dissecting Clonal Hematopoiesis in Tissues of Patients with Classic Hodgkin Lymphoma

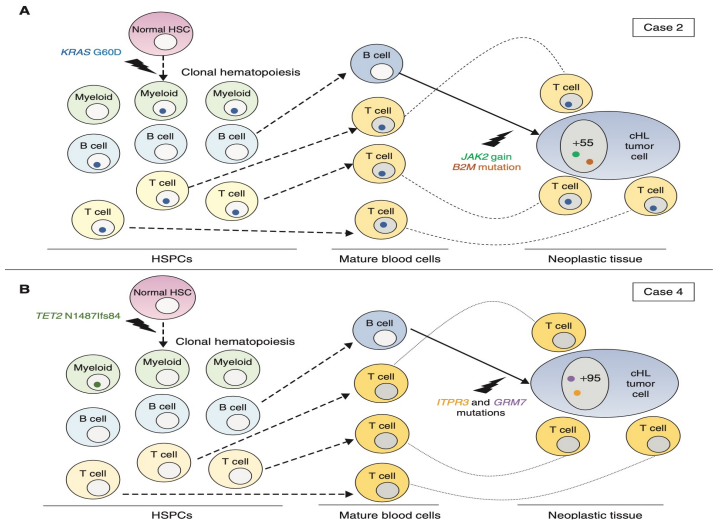
Alessandra Venanzi, Andrea Marra, Gianluca Schiavoni, Sara G. Milner, Roberto Limongello, Alessia Santi, Valentina Pettirossi, Simona Ultimo, Luisa Tasselli, Alessandra Pucciarini, Lorenza Falini, Sofia Sciabolacci, Maria Paola Martelli, Paolo Sportoletti, Stefano Ascani, Brunangelo Falini, and Enrico Tiacci

Table 1. Prevalence and tissue distribution of clonal hematopoiesis in patients ($n = 40$) with cHL

CH present	Years of age	Pt.#	Time of sampling	Progressed after first-line chemotherapy	Gene mutation	VAF in whole blood	VAF in microdissected: Reactive lymphoid cells	VAF in microdissected: HRS cells	VAF in whole tissue section	AML onset: VAF in bone marrow	AML remission: VAF in blood T cells	AML remission: VAF in blood B cells
NO ($n = 35$)	Median 35 Range 15–75											
YES ($n = 5$)	30	Case 2	2nd relapse	YES	*KRAS* G60D	NA	45.9%	ND	22.9%			
	83	Case 3	Onset	Not evaluable	*CBL* G375S	NA	2.5%	ND	NA			
	81	Case 4	Onset	NO	*TET2* N1487Ifs84	3.2%	ND	ND	NA			
	73	Case 5	Onset	YES	*DNMT3A* R882H	NA	NA	NA	32.4%			
					TET2 Q1274[a]				22.3%			
			1st relapse		*DNMT3A* R882H	NA	30%	43%	37.9%			
					TET2 Q1274[a]		8.4%	31.1%	26.9%			
	45	Case 1	Onset	YES	*DNMT3A* R882H	47%	16.4%	ND	12.2%	45.2%	6.9%	48%
					NPM1 W288CfsTer12	ND				40.6%	ND	
					PTPN11 E76K	ND				25.7%	ND	
					FLT3 ITD	NA				0.14[a]	NA	
					FLT3 ITD	NA				0.11[a]	NA	
					STAT6 N417Y	NA	ND	36.9%	NA	NA		
					STAT6 D419H			35.7%				
					SOCS1 P83Afs*25			98.6%				

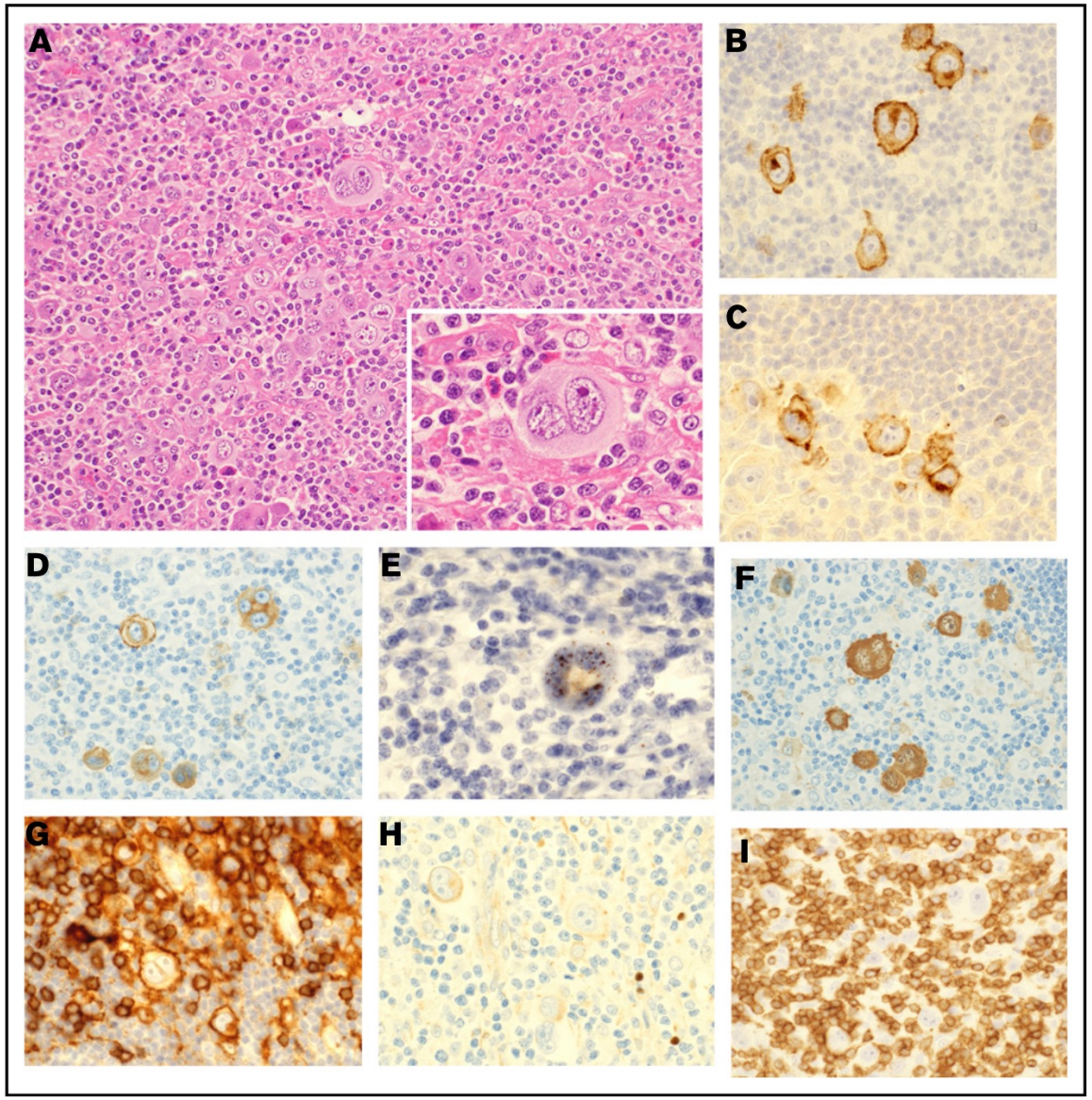
Abbreviations: CH, clonal hematopoiesis; NA, not available; ND, not detected.
[a]Mutant/wild-type ratio by fragment length analysis.

- 40 cHL cases by sequencing microdissected tumor cells and matched normal cells from blood and/or lymph nodes.
- 5 pts patients had blood and/or tissue clonal hematopoiesis.
- In three of five patients (all failing first-line therapy), clonal hematopoiesis spread through the tissue microenvironment extensively,
- mutantations *DNMT3A*R882H, *KRAS*G60D, and *DNMT3A*R882H+*TET2*Q1274* in 33%, 92%, and 60% of non-neoplastic cells, respectively.
- In case with *DNMT3A/TET2*-mutant clonal hematopoiesis seeded the neoplastic clone, which was infected by the Epstein–Barr virus and showed almost no other somatic mutations exome-wide.
- In *DNMT3A*R882H -mutant clonal hematopoiesis did not originate the neoplastic clone despite dominating the blood and B-cell lineage (~94% leukocytes; ~96% mature blood B cells), yet led to *NPM1*-mutated acute myeloid leukemia 6 years after therapy for cHL.
- TCR policlonal



SigNifiCANCe:

Clonal hematopoiesis can be present in the cHL tissue, can give rise to the tumor clone, and can spread to large parts of its microenvironment. Even when massive, clonal hematopoiesis does not always give rise to the neoplastic clone of multiple myeloid and lymphoid neoplasms occurring in the same patient.



REGULAR ARTICLE

blood advances

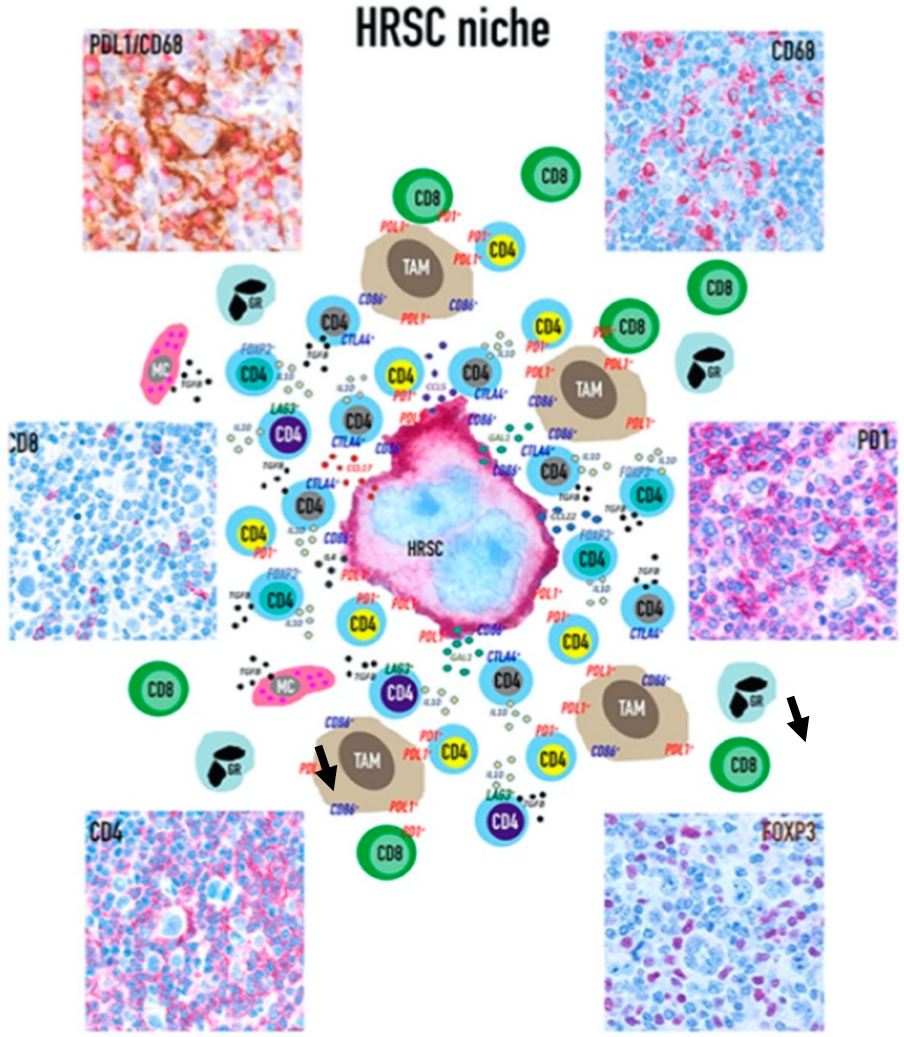
Clinicopathological features of adult T-cell leukemia/lymphoma with HTLV-1–infected Hodgkin and Reed-Sternberg–like cells

Kennosuke Karube,[1] Mitsuyoshi Takatori,[1] Shugo Sakihama,[1] Yuma Tsuruta,[2] Takashi Miyagi,[3] Kazuho Morichika,[4] Sakiko Kitamura,[4] Norihiro Nakada,[5] Masaki Hayashi,[6] Shohei Tomori,[6] Iwao Nakazato,[7] Kazuiku Ohshiro,[8] Naoki Imaizumi,[9] Yara Yukie Kikuti,[10] Naoya Nakamura,[10] Satoko Morishima,[4] Hiroaki Masuzaki,[4] and Takuya Fukushima[11]

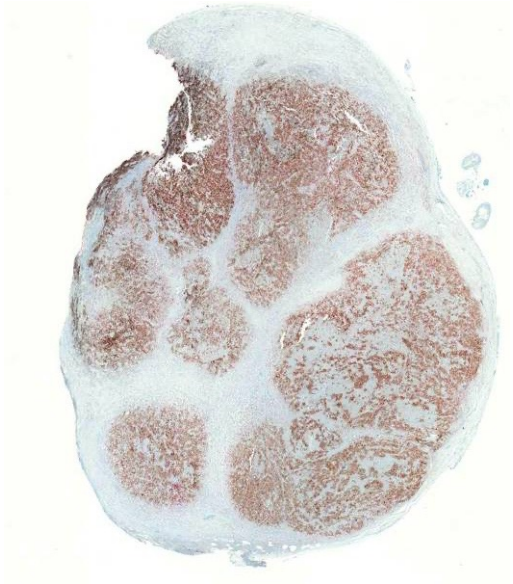
Figure 1. Pathological findings of lymph nodes in ATLL with HTLV-1–infected HRS-like cells. (A) Lymph nodes of case 7 were effaced by infiltration of HRS-like cells (inset) in a background of lymphocytes, histiocytes, and eosinophils (hematoxylin and eosin staining). (B-H) The HRS-like cells were positive for CD30 (B), CD15 (C), CD25 (D), HBZ-ISH (E), fascin (F), and CD4 (G) and negative for PAX5 (H). Most of the infiltrating small lymphocytes were T cells positive for CD3 (I) and negative for HBZ-ISH (E). Original magnification ×200 (A) and ×400 (A, inset, and B-I).

Key Points

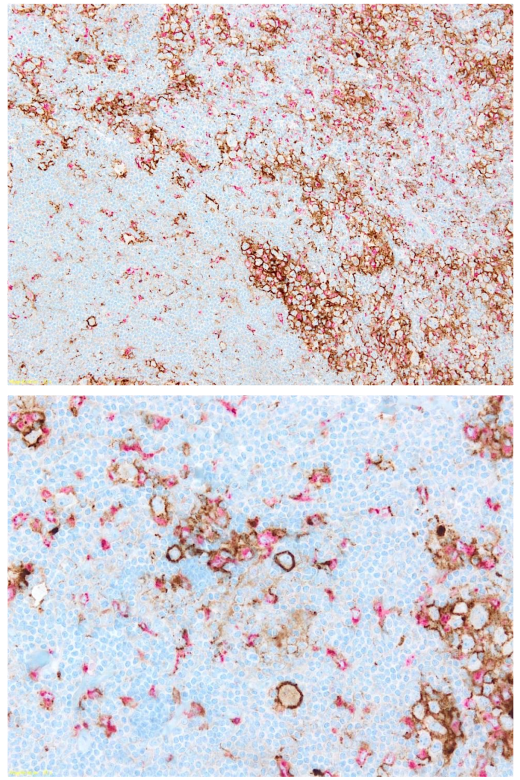
- ATLL with HTLV-1–infected HRS-like cells is a new pathological variant of ATLL, distinct from conventional Hodgkin-like variant of ATLL.
- Diffuse HBZ-ISH positivity and negativity for PAX5 and EBV are key features distinguishing this variant from other morphological mimics.

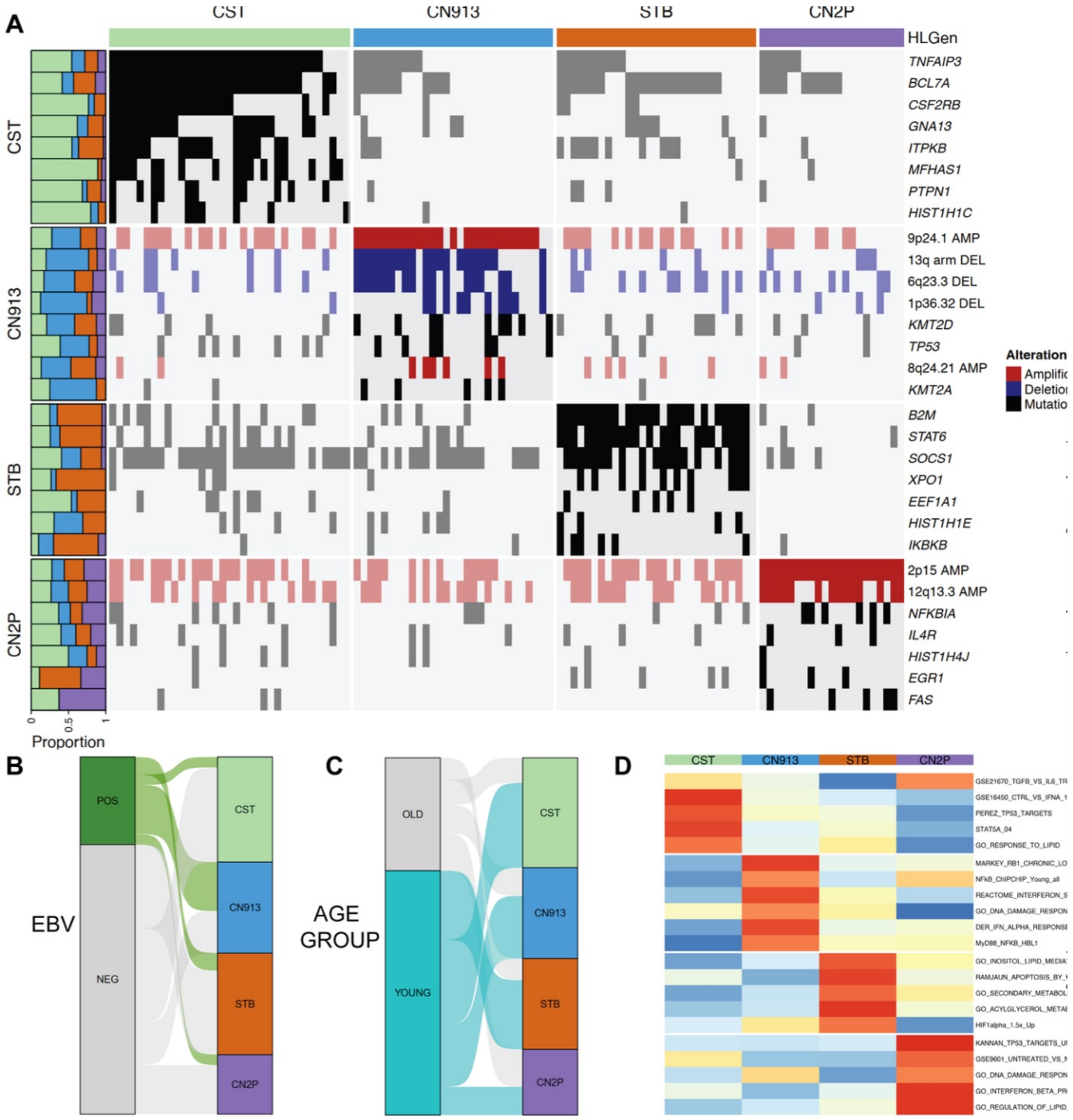


- activated and differentiated T cell subsets: regulatory T cells (CTLA4^{+} or LAG3^{+}) activated/proliferating CD4^{+} T cells, exhausted CD8 $^{+}$ T cells, decrease in less differentiated naive T cells.
- monocytes/macrophages were significantly expanded, particularly in EBV+ cHL
- In contrast, fibroblasts, plasma cells, and plasmacytoid dendritic cells were depleted from HRS cell neighborhoods



CD68/PD-L1(28-8)





Aoki et al Cancer Discovery 2026

CHL subgroups:

CST (characteristic mutations in CSF2RB and TNFAIP3, 31%), *younger age,* and up-regulation of the STAT5 pathway.

CN913 (copy number gain of 9p24 and 13q deletion 25%), characterized by significant upregulation of IFNγ and nuclear factor-κB (NF-κB) signaling pathways, and in 79% of cases *EBV-positive*

STB (mutations in STAT6 and B2M, 25%) and upregulation of a TGFb signature in HRS cells, and 40% of relapsed HL samples were classified as STB; exhibited a trend toward inferior PFS, consistent with its slight enrichment in *relapsed biopsy*

CN2P (copy number gains in 2p15, 18%) included samples from *mostly older patients* (p<0.001, Odds Ratio 0.42), and showed significant upregulation of a DNA repair and a TP53 target signature

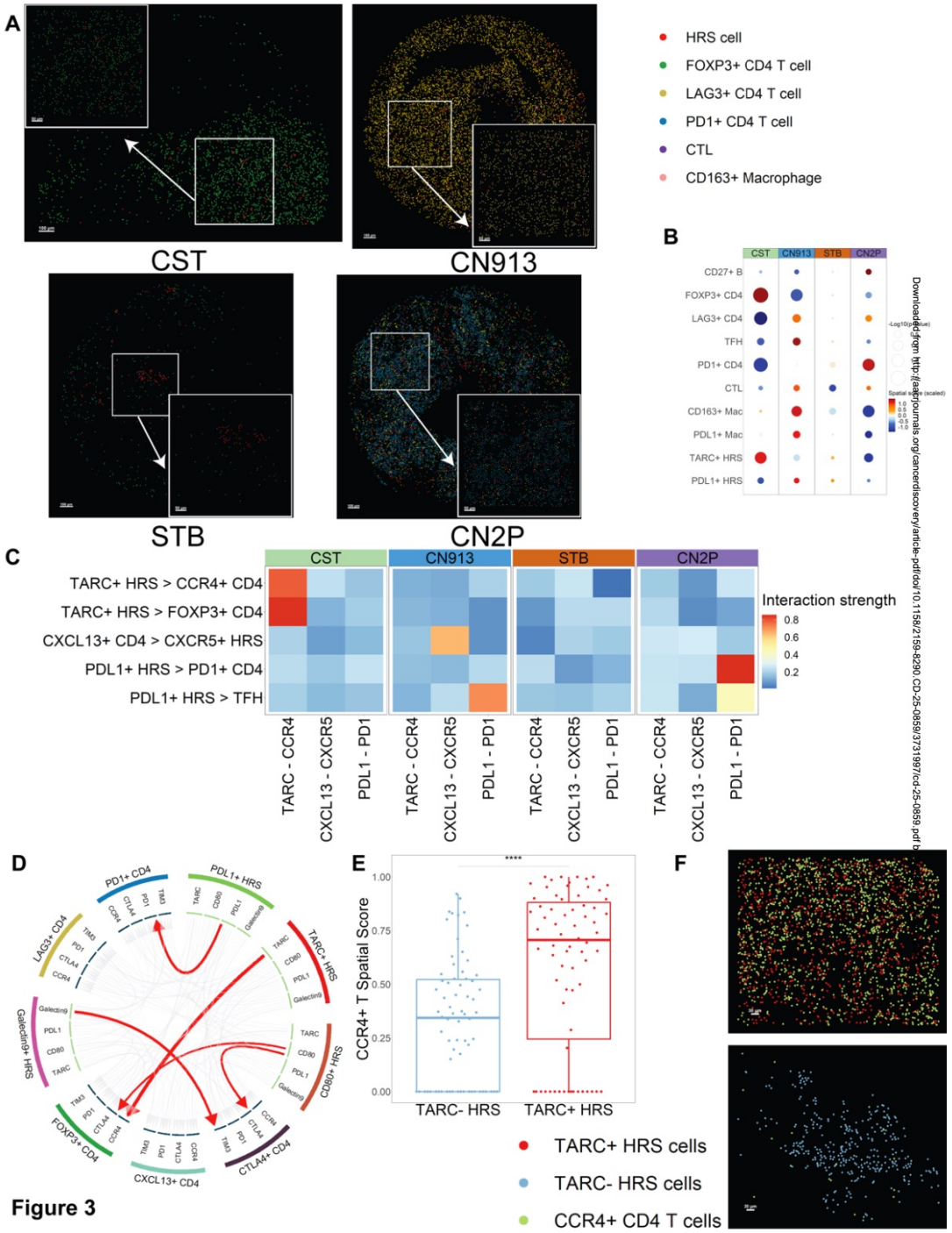


Figure 3

CST significant enrichment of FOXP3$^+$ regulatory T cells (Tregs) and CCR4$^+$ T cells.
interaction of CCL17 (TARC)-positive HRS cells with CCR4$^+$CD4$^+$ T cells

CN913 subgroup showed a significant enrichment of LAG3$^+$CD4$^+$ T cells. Interactions with PDL1$^+$ macrophage population surrounding HRS cells where PDL1 copy number gains in HRS cells were frequent

CN2P enrichment of PD1$^+$CD4$^+$ T cells; interactions between PD-L1$^+$ HRS cells and PD1$^+$CD4$^+$ T cells

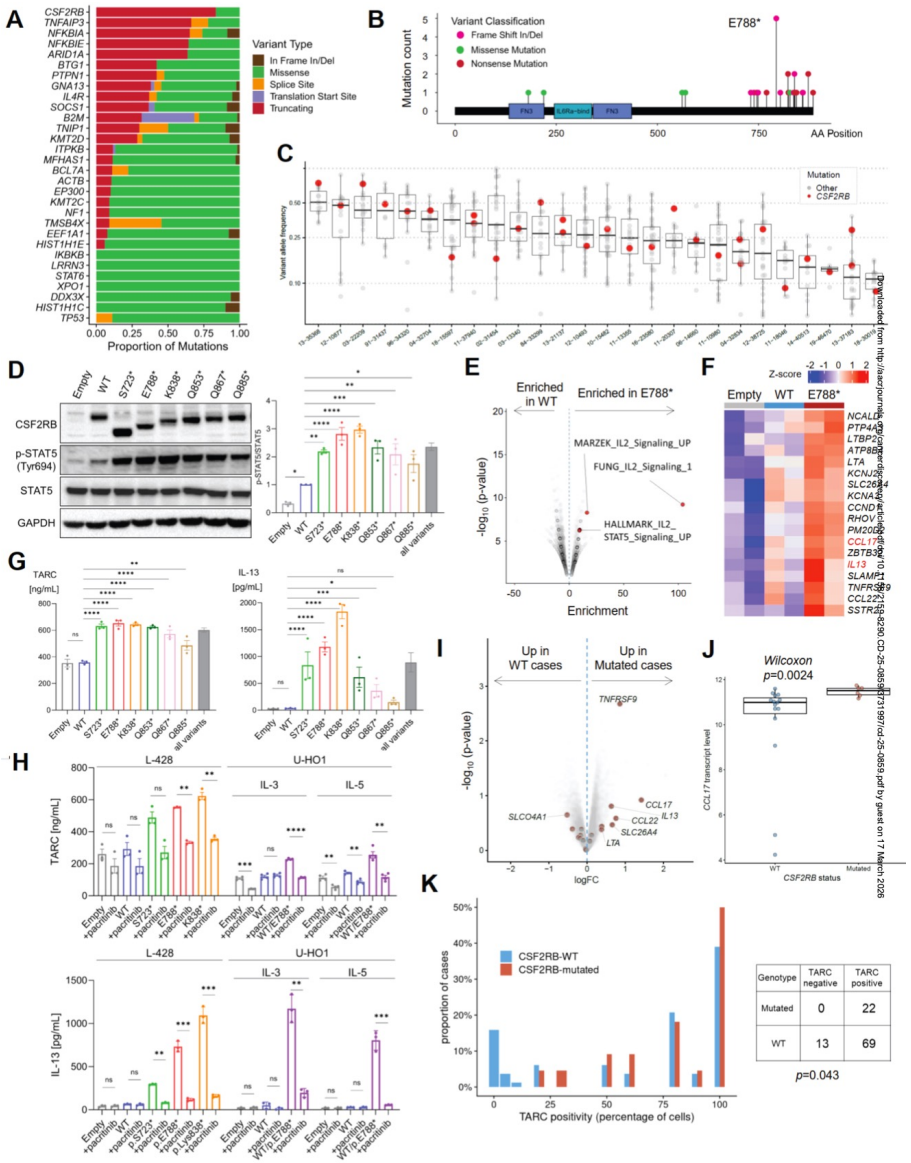
STB subgroup, is characterized by the presence of B2M mutations, immune-cold microenvironment (less CD8+/GZB cytotoxic ly); interactions between CXCR5$^+$ HRS cells and CXCL13$^+$ macrophages; Interactions of Galectin-9$^+$ HRS cells with TIM3$^+$ macrophages

Importantly, each significant cell-to-cell interaction was only observed within each distinct molecular subgroup

The strong association between genetic subgroups and distinct TME ecosystems suggests opportunities for immunotherapeutic Targeting

CST subgoup (*younger age*)

- CSF2RB [β common chain receptor (βc)], is a component of cytokine receptors with specificity to IL-3, IL-5, and GM-CSF, which activate signaling pathways, such as JAK2-STAT5
- gain-of function phenotype of CSF2RB truncating mutations contributes to an increased Treg infiltration through the TARC-CCR4 axis
- CSF2RB mutations are virtually absent in other major B-cell
- selective JAK2 inhibition reversed the gain-of-function phenotype of CSF2RB mutations, indicating the potential benefit of targeting this pathway in the CST molecular subtype that encompasses tumors with CSF2RB mutations.
- This potential subtype-specificity of JAK2 inhibition might in part also explain the only marginal efficacy of JAK2 inhibitors observed in unselected and molecularly uncharacterized CHL patients in clinical trials .
- Recent studies have suggested that JAK inhibition may enhance the efficacy of immunotherapy in HL



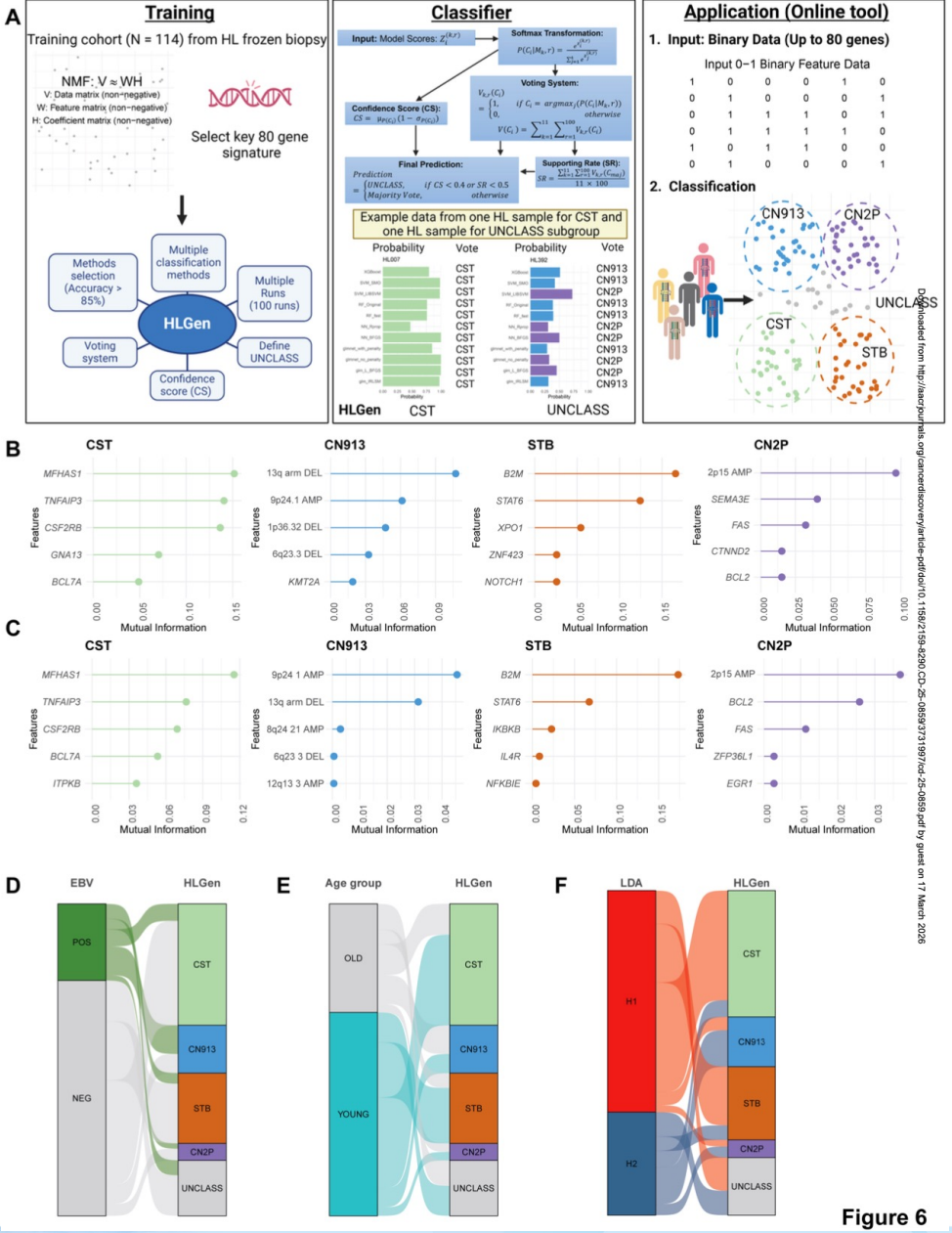
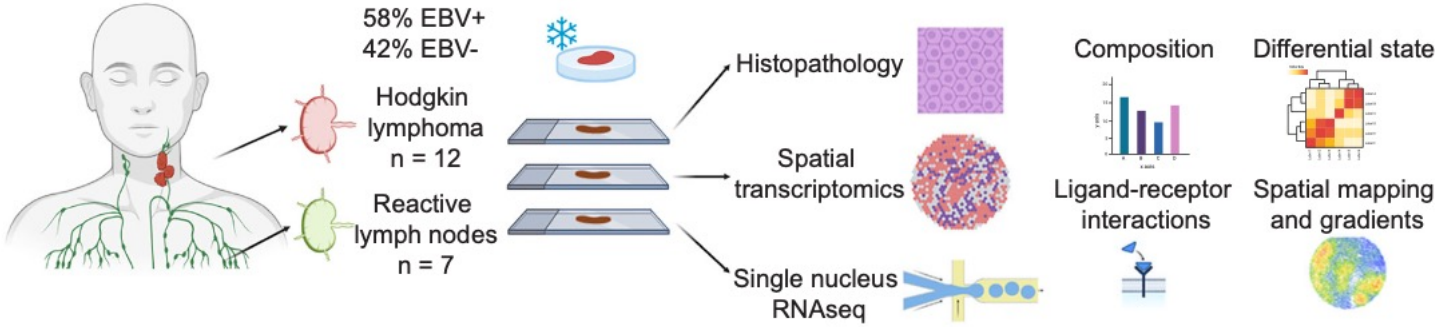


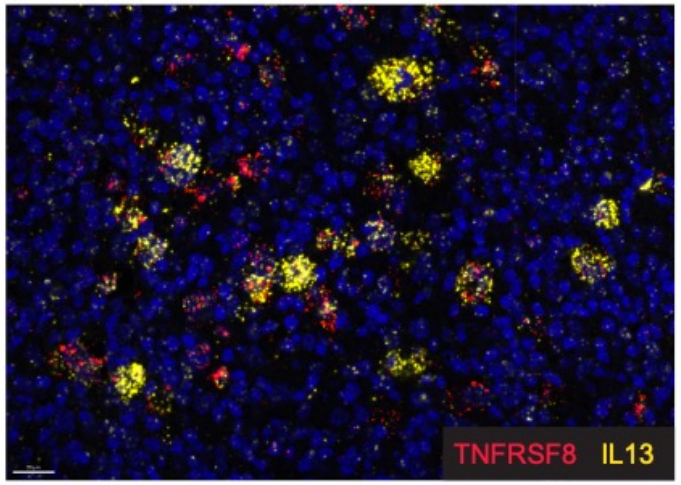
Figure 6

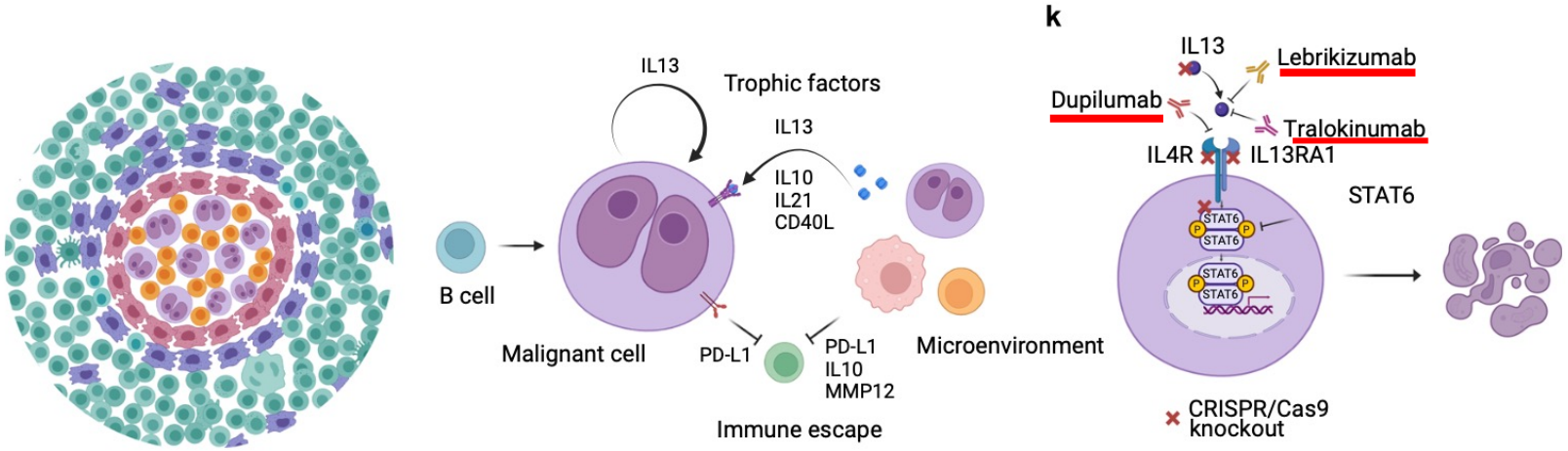
The molecular classification system developed in this study, named HLGen, further improves biology-informed disease taxonomies, with the goal to guide treatment strategies and inform prognosis.

HLGen molecular aberration-based classification tool and requires only binary input data of up to 80 gene features

HLGen is available as an online tool (https://shiny.bcgsc.ca/HLGen/) for further validation in routine clinical practice and future clinical trials.

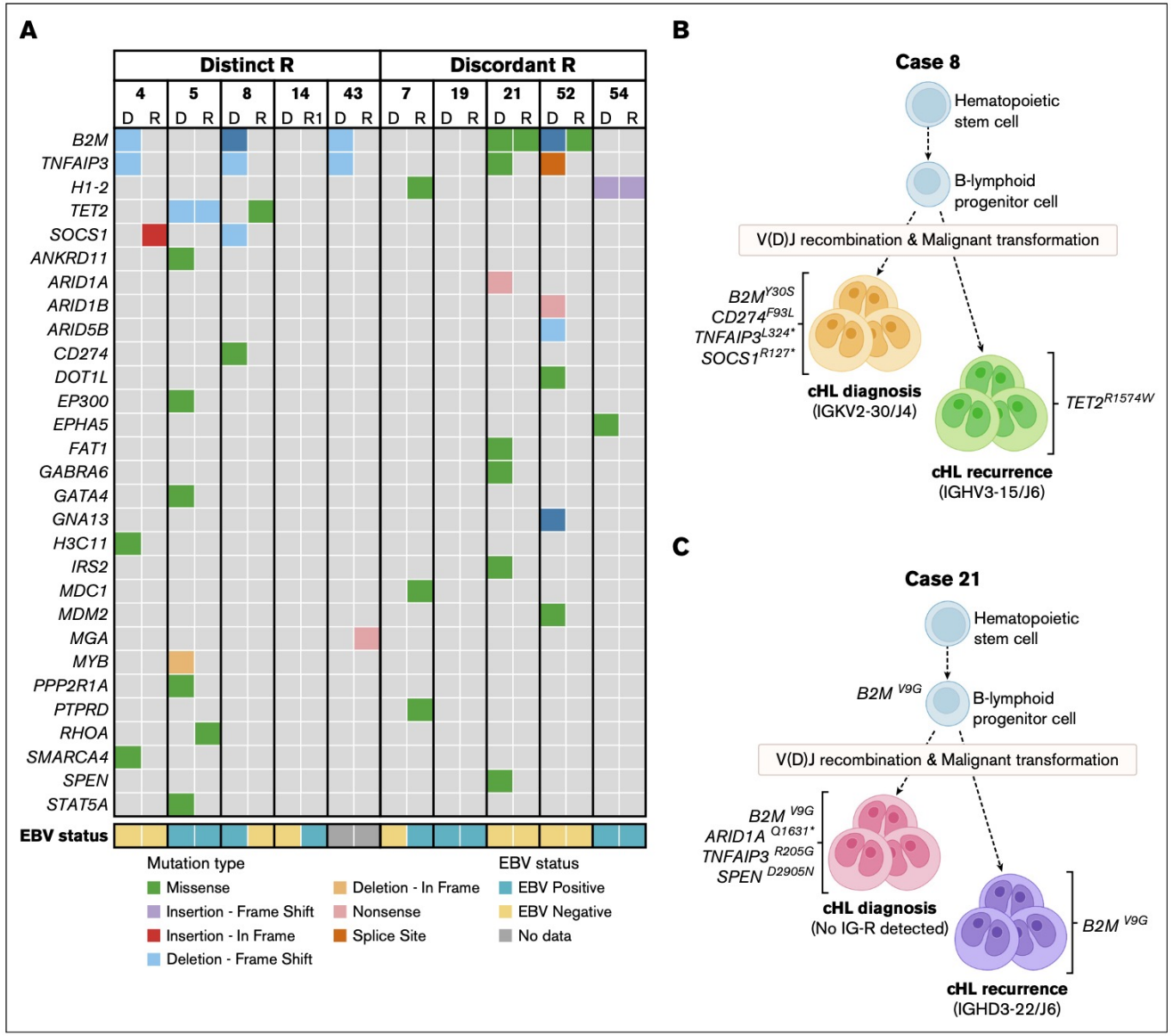






- Spatial analysis nominates IL13 as a candidate survival factor.
- Recombinant IL13 augments malignant cell growth in vitro, and genome-wide loss-of-function screens across >1000 human cancer cell lines identify IL4R and IL13RA1, heterodimeric components of the IL13 receptor, as uniquely essential in Hodgkin lymphoma.
- Importantly, blocking antibodies phenocopy genetic inactivation, which are already FDA-approved.
- These findings provide a biological rationale for testing IL13-directed therapies,, in Hodgkin lymphoma.

Shanmugan Nature Communications (2026)



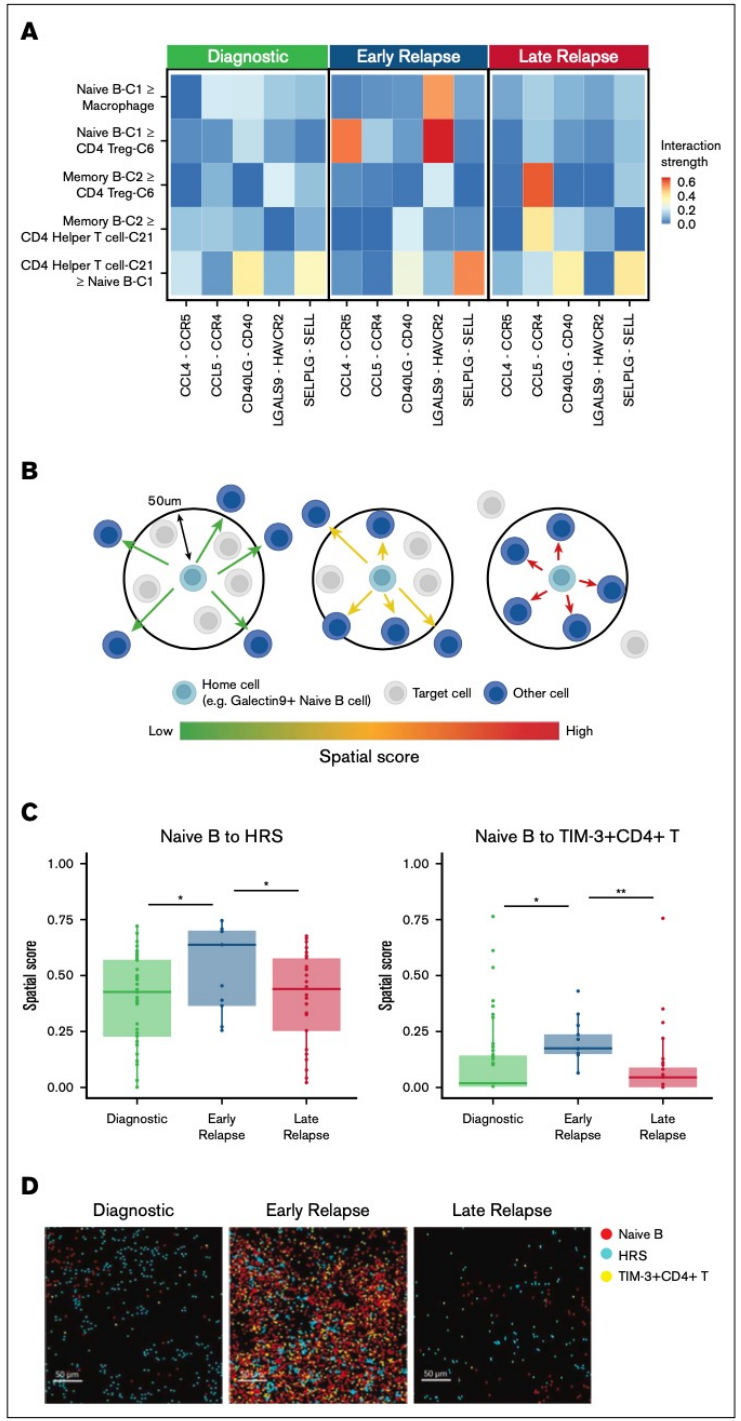
REGULAR ARTICLE

blood advances

A significant proportion of classic Hodgkin lymphoma recurrences represents clonally unrelated second primary lymphoma

Diede A. G. van Bladel,[1] Wendy B. C. Stevens,[2] Leonie I. Kroeze,[1] Ruben A. L. de Groen,[3] Fleur A. de Groot,[3] Jessica L. M. van der Last-Kempkes,[1] Madeleine R. Berendsen,[1] Jos Rijntjes,[1] Jeroen A. C. W. Luijks,[1] Irina Bonzheim,[4] Ellen van der Spek,[5] Wouter J. Plattel,[6] Johannes F. M. Pruijt,[7] Susan D. P. W. M. de Jonge-Peeters,[8] Gerjo A. Velders,[9] Chantal Lensen,[10] Esther R. van Bladel,[11] Birgit Federmann,[4,12] Brigiet M. Hoevenaars,[13] Agata Pastorczak,[14] Jutte van der Werff ten Bosch,[15,16] Joost S. P. Vermaat,[3] Peet T. G. A. Nooijen,[17] Konnie M. Hebeda,[1] Falko Fend,[4] Arjan Diepstra,[18] J Han J. M. van Krieken,[1] Patricia J. T. A. Groenen,[1] Michiel van den Brand,[19] and Blanca Scheijen[1]

in-depth molecular analysis demonstrates the occurrence of second de novo cHL in approximately one-third of patients with cHL and ~60% of patients with cHL, with a time to recurrence of >2 years after primary cHL diagnosis



identified distinct shifts in B-cell populations, particularly an enrichment of naïve B cells and a reduction of memory B cells in early-relapse CHL compared to late-relapse and newly diagnosed CHL.

naïve B cells in early-relapse samples exhibited high expression of galectin-9, which binds to TIM-3 on Tregs

Cell-cell interaction analysis revealed the importance of interactions between galectin-9^{+} naïve B cells and *TIM3*$^{+}$ Tregs in the early-relapse setting.

Spatial analysis by imaging mass cytometry confirmed close proximity of galectin-9–positive naïve B cells with TIM-3^{+}CD4^{+} T cells and HRS cells, pointing to their role in shaping an immunosuppressive niche.

Key Points

- Naïve B cells expressing *LGALS9* (galectin-9) are distinctly increased in early-relapse CHL compared to diagnostic and late-relapse samples.
- Galectin-9–positive naïve B cells engage with TIM-3^{+} T cells, potentially contributing to an immunosuppressive TME in early-relapse CHL.

Yin et al blood advances 2026


Thanks
Thank you very much
I really appreciate it
You are the best
I owe you one
I owe you big time
You re great
You re awesome
You re too kind
You re a life saver
Please accept my best thanks
Thanks a million
Thanks a bunch
Thanks a lot
Thanks a ton
I humbly thank you
You saved my day
You made my day
You are an angel
Thanks so much
Thanks for everything
I don t know what to say!
Thank you for everything
It s very kind of you
I thank you from the bottom of my heart
I can t thank you enough
It was so awesome of you
How can I ever thank you enough
I do not know what I would do without you
I cannot express my appreciation
All I can say is, Thanks!
I thank you most warmly
I m so grateful
I couldn t have done it without you
I really want to thank you for your help
I wish to thank everyone who pitched in
Many thanks
You re a dear
I really appreciate your time
I appreciate your time
Words can t describe how thankful I am
I really appreciate everything you ve done
You ve saved my life
How can I ever possibly thank you
What would I do without you?
Accept my endless gratitude
I m really grateful for your help
Oh, you shouldn t have!