Hospital Universitario Fundación Jiménez Díaz
Grupo quirónsalud

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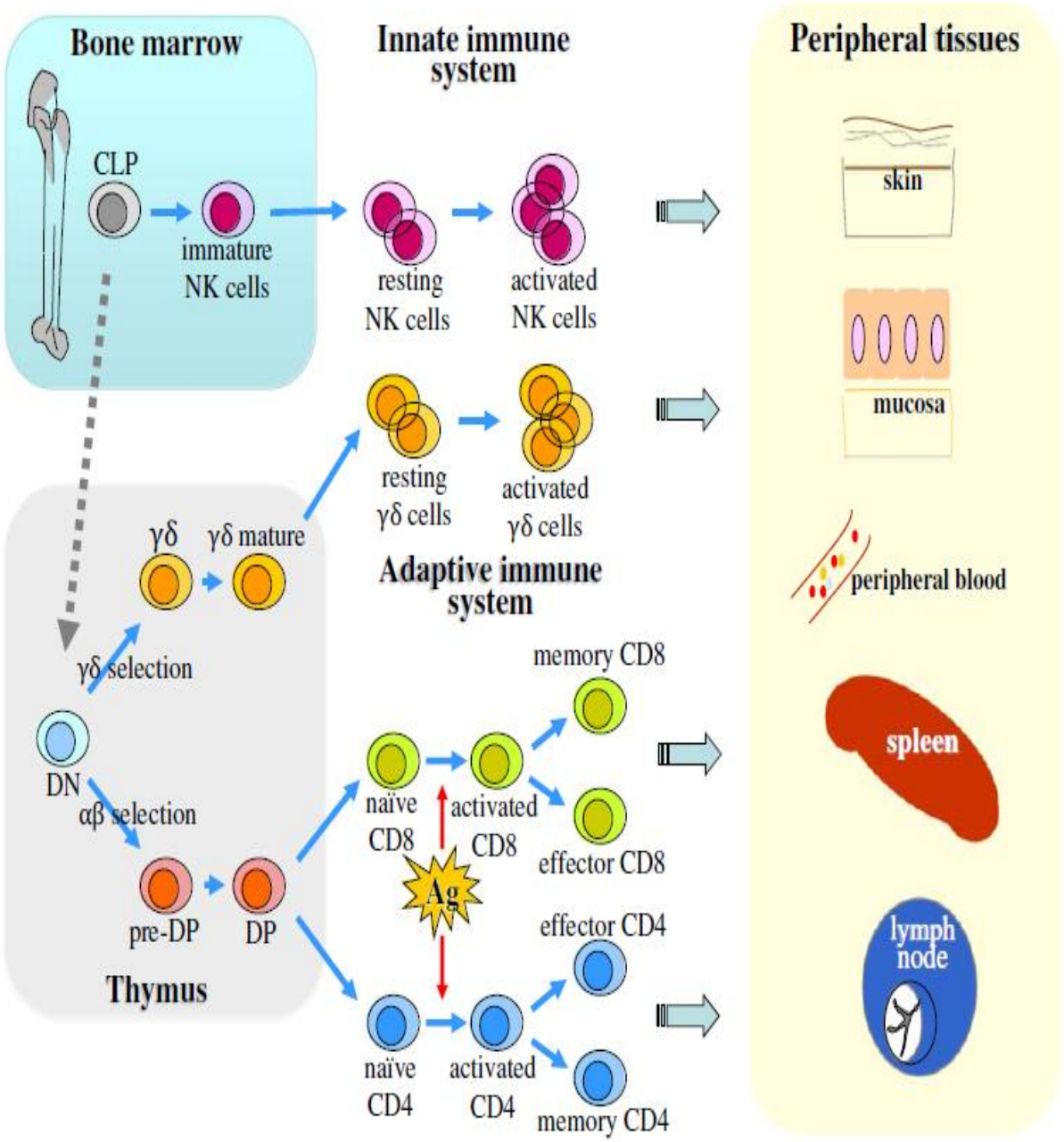
Socorro Maria Rodriguez Pinilla
FJD, Madrid



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REVIEW ARTICLE OPEN

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LYMPHOMA

The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms

Rita Alaggio[1], Catalina Amador[2], Ioannis Anagnostopoulos[3], Ayoma D. Attygalle[4], Iguaracyra Barreto de Oliveira Araujo[5], Emilio Berti[6], Govind Bhagat[7], Anita Maria Borges[8], Daniel Boyer[9], Mariarita Calaminici[10], Amy Chadburn[11], John K. C. Chan[12], Wah Cheuk[12], Wee-Joo Chng[13], John K. Choi[14], Shih-Sung Chuang[15], Sarah E. Coupland[16], Magdalena Czader[17], Sandeep S. Dave[18], Daphne de Jong[19], Ming-Qing Du[20]✉, Kojo S. Elenitoba-Johnson[21], Judith Ferry[22]✉, Julia Geyer[11], Dita Gratzinger[23], Joan Guitart[24], Sumeet Gujral[25], Marian Harris[26], Christine J. Harrison[27], Sylvia Hartmann[28], Andreas Hochhaus[29], Patty M. Jansen[30], Kennosuke Karube[31], Werner Kempf[32], Joseph Khoury[33], Hiroshi Kimura[34], Wolfram Klapper[35], Alexandra E. Kovach[36], Shaji Kumar[37], Alexander J. Lazar[38], Stefano Lazzi[39], Lorenzo Leoncini[39], Nelson Leung[40], Vasiliki Leventaki[41], Xiao-Qiu Li[42], Megan S. Lim[21], Wei-Ping Liu[43], Abner Louissaint Jr.[22], Andrea Marcogliese[44], L. Jeffrey Medeiros[33], Michael Michal[45], Roberto N. Miranda[33], Christina Mitteldorf[46], Santiago Montes-Moreno[47], William Morice[48], Valentina Nardi[22], Kikkeri N. Naresh[49], Yasodha Natkunam[23], Siok-Bian Ng[50], Ilske Oschlies[35], German Ott[51]✉, Marie Parrens[52], Melissa Pulitzer[53], S. Vincent Rajkumar[54], Andrew C. Rawstron[55], Karen Rech[48], Andreas Rosenwald[3], Jonathan Said[56], Clémentine Sarkozy[57], Shahin Sayed[58], Caner Saygin[59], Anna Schuh[60], William Sewell[61], Reiner Siebert[62]✉, Aliyah R. Sohani[22], Reuben Tooze[63], Alexandra Traverse-Glehen[64], Francisco Vega[33], Beatrice Vergier[65], Ashutosh D. Wechalekar[66], Brent Wood[36], Luc Xerri[67] and Wenbin Xiao[53]

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Hepatosplenic T-cell lymphoma
Hepatosplenic T-cell lymphoma
Anaplastic large cell lymphoma
ALK-positive anaplastic large cell lymphoma
ALK-negative anaplastic large cell lymphoma
Breast implant-associated anaplastic large cell lymphoma
Nodal T-follicular helper (TFH) cell lymphoma
Nodal TFH cell lymphoma, angioimmunoblastic-type
Nodal TFH cell lymphoma, follicular-type
Nodal TFH cell lymphoma, NOS
Other peripheral T-cell lymphomas
Peripheral T-cell lymphoma, not otherwise specified
EBV-positive NK/T-cell lymphomas
EBV-positive nodal T- and NK-cell lymphoma

blood® Special Report

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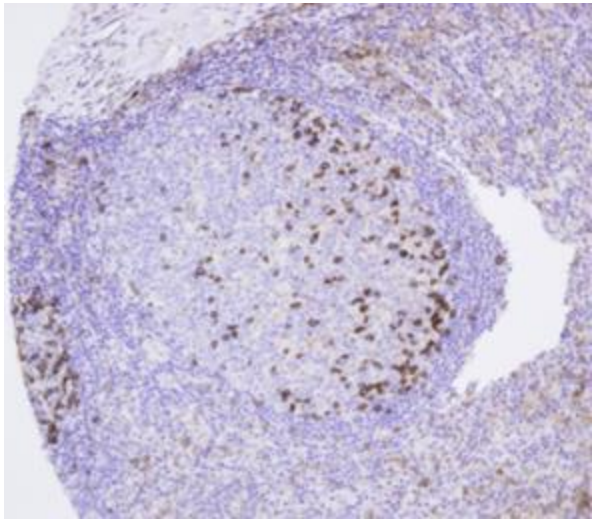
The International Consensus Classification of Mature Lymphoid Neoplasms: a report from the Clinical Advisory Committee

Elias Campo,[1] Elaine S. Jaffe,[2] James R. Cook,[3] Leticia Quintanilla-Martinez,[4] Steven H. Swerdlow,[5] Kenneth C. Anderson,[6] Pierre Brousset,[7] Lorenzo Cerroni,[8] Laurence de Leval,[9] Stefan Dirnhofer,[10] Ahmet Dogan,[11] Andrew L. Feldman,[12] Falko Fend,[4] Jonathan W. Friedberg,[13] Philippe Gaulard,[14,15] Paolo Ghia,[16] Steven M. Horwitz,[17] Rebecca L. King,[12] Gilles Salles,[17] Jesus San-Miguel,[18] John F. Seymour,[19] Steven P. Treon,[6] Julie M. Vose,[20] Emanuele Zucca,[21] Ranjana Advani,[22] Stephen Ansell,[23]

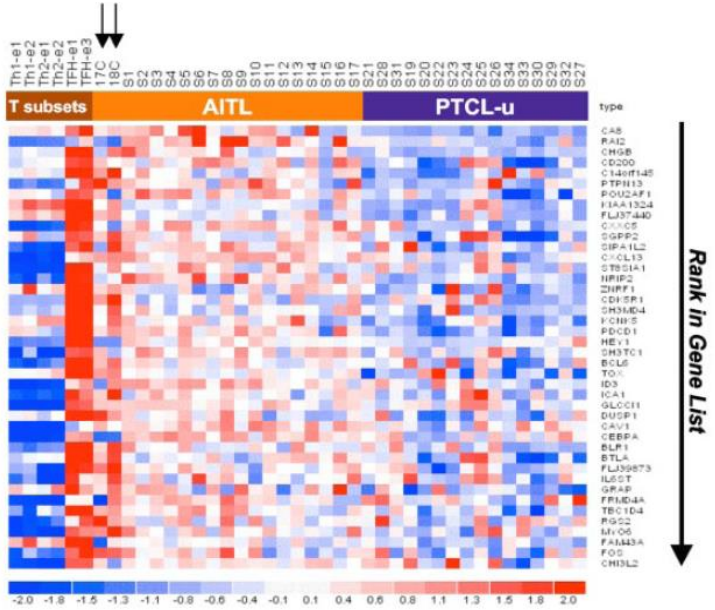
Primary cutaneous small/medium CD4$^+$ T-cell lymphoproliferative disorder
Subcutaneous panniculitis-like T-cell lymphoma
Primary cutaneous gamma-delta T-cell lymphoma
Primary cutaneous acral CD8$^+$ T-cell lymphoproliferative disorder*
Primary cutaneous CD8$^+$ aggressive epidermotropic cytotoxic T-cell lymphoma
Peripheral T-cell lymphoma, NOS
Follicular helper T-cell lymphoma*
Follicular helper T-cell lymphoma, angioimmunoblastic type (angioimmunoblastic T-cell lymphoma)
Follicular helper T-cell lymphoma, follicular type
Follicular helper T-cell lymphoma, NOS
Anaplastic large cell lymphoma, ALK positive
Anaplastic large cell lymphoma, ALK negative
Breast implant–associated anaplastic large cell lymphoma

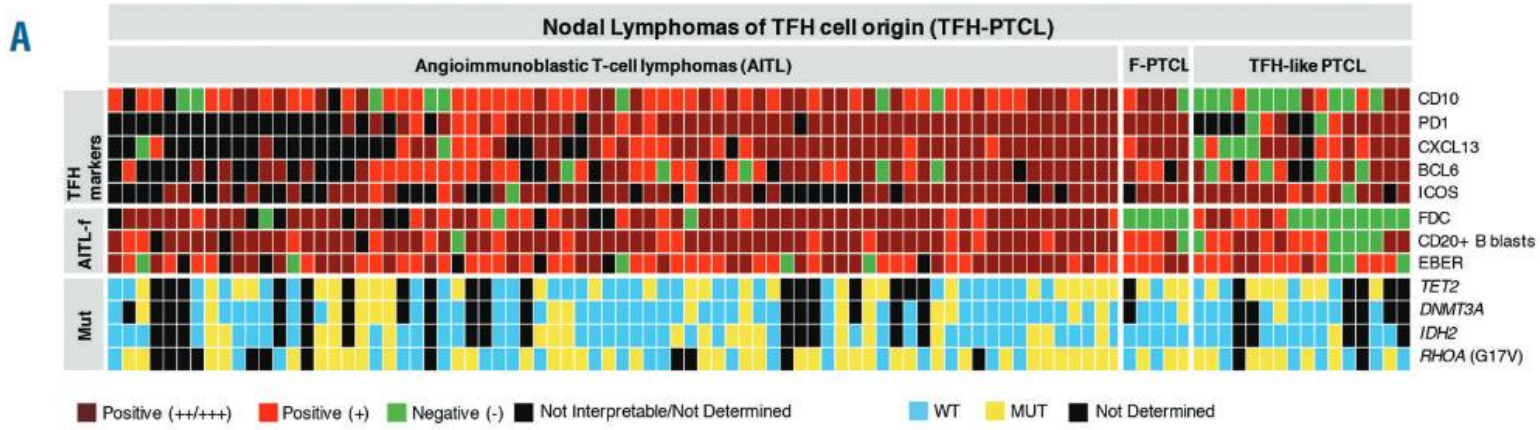
haematologica 2017; 102:e148

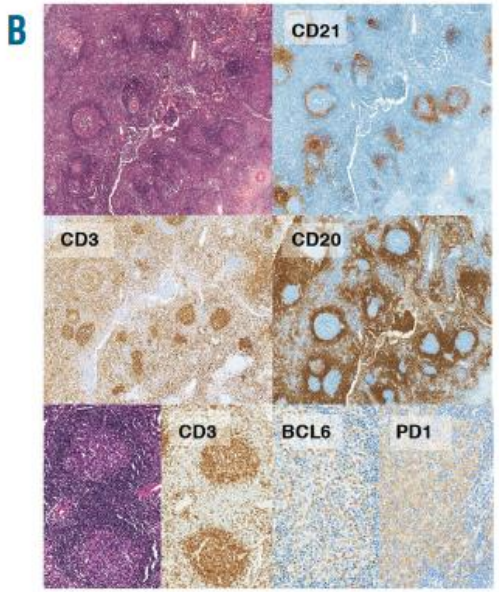
LETTERS TO THE EDITOR

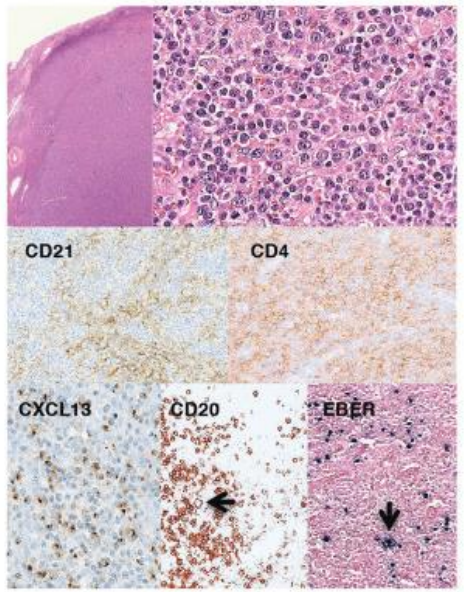


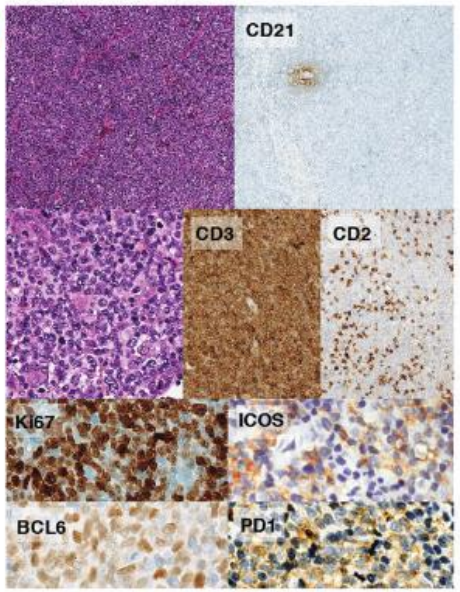
De Leval L, et al; Blood ; 2007.











www.oncotarget.com Oncotarget, 2018, Vol. 9, (No. 22), pp: 16124-16133

Research Paper

Overlap at the molecular and immunohistochemical levels between angioimmunoblastic T-cell lymphoma and a subgroup of peripheral T-cell lymphomas without specific morphological features

Rebeca Manso[1], Julia González-Rincón[2,5], Manuel Rodríguez-Justo[3], Giovanna Roncador[4], Sagrario Gómez[2], Margarita Sánchez-Beato[2], Miguel A. Piris[1,5] and Socorro M. Rodríguez-Pinilla[1,5]

[1]Pathology Department, Fundación Jiménez Díaz, UAM, Madrid, Spain

[2]Instituto Investigación Sanitaria Puerta de Hierro-Segovia de Arana (IDIPHIM), Madrid, Spain

[3]UCL Cancer Institute, Department of Research Pathology, London, UK

[4]Monoclonal Antibodies Unit, Biotechnology Programme, Spanish National Cancer Research Centre (CNIO), Madrid, Spain

[5]Centro de Investigación Biomédica en Red Cáncer (CIBERONC), Madrid, Spain

Correspondence to: *Socorro M. Rodríguez-Pinilla,* ***email:*** *smrodriguez@fjd.es*

Keywords: *AITL; PTCL; T_{FH}-phenotype; IHQ; NGS*

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ABSTRACT

The overlap of morphology and immunophenotype between angioimmunoblastic T-cell lymphoma (AITL) and other nodal peripheral T-cell lymphomas (n-PTCLs) is a matter of current interest whose clinical relevance and pathogenic background have not been fully established. We studied a series of 98 n-PTCL samples (comprising 57 AITL and 41 PTCL-NOS) with five T_{FH} antibodies (CD10, BCL-6, PD-1, CXCL13, ICOS), looked for mutations in five of the genes most frequently mutated in AITL (*TET2, DNMT3A, IDH2, RHOA* and *PLCG1*) using the Next-Generation-Sequencing Ion Torrent platform, and measured the correlations of these characteristics with morphology and clinical features. The percentage of mutations in the *RHOA* and *TET2* genes was similar (23.5% of cases). *PLCG1* was mutated in 14.3%, *IDH2* in 11.2% and *DNMT3A* in 7.1% of cases, respectively. In the complete series, mutations in *RHOA* gene were associated with the presence of mutations in *IDH2, TET2* and *DNMT3A* ($p < 0.001$, $p = 0.043$, and $p = 0.029$, respectively). Fourteen cases featured *RHOA* mutations without *TET2* mutations. A close relationship was found between the presence of these mutations and a T_{FH}-phenotype in AITL and PTCL-NOS patients. Interestingly, BCL-6 expression was the only T_{FH} marker differentially expressed between AITL and PTCL-NOS cases. There were many fewer mutated cases than there were cases with a T_{FH} phenotype. Overall, these data suggest alternative ways by which neoplastic T-cells overexpress these proteins. On the other hand, no clinical or survival differences were found between any of the recognized subgroups of patients with respect to their immunohistochemistry or mutational profile.

REGULAR ARTICLE

blood advances

Peripheral T-cell lymphoma: molecular profiling recognizes subclasses and identifies prognostic markers

Marta Rodríguez,[1,2,*] Ruth Alonso-Alonso,[1,2,*] Laura Tomás-Roca,[1,*] Socorro M. Rodríguez-Pinilla,[1,2] Rebeca Manso-Alonso,[1] Laura Cereceda,[1,2] Jennifer Borregón,[1] Teresa Villaescusa,[3] Raúl Córdoba,[2,3] Margarita Sánchez-Beato,[2,4] Ismael Fernández-Miranda,[4] Isabel Betancor,[1] Carmen Bárcena,[5] Juan F. García,[2,6] Manuela Mollejo,[2,7] Mónica García-Cosio,[2,8] Paloma Martín-Acosta,[2,9] Fina Climent,[10] Dolores Caballero,[11] Lorena de la Fuente,[12,13] Pablo Mínguez,[12-14] Linda Kessler,[15] Catherine Scholz,[15] Antonio Gualberto,[15] Rufino Mondéjar,[2,16] and Miguel A. Piris[1,2]

[1]Pathology Department, Instituto de Investigación Sanitaria Fundación Jiménez Díaz, Madrid, Spain; [2]Centro de Investigación Biomédica en Red de Cáncer (CIBERONC), ISCIII, Madrid, Spain; [3]Lymphoma Unit, Department of Hematology, Fundación Jiménez Díaz University Hospital, Health Research Institute IIS-FJD, Madrid, Spain; [4]Lymphoma Research Group, Medical Oncology Department, Instituto de Investigación Sanitaria Puerta de Hierro-Segovia de Arana, Madrid, Spain; [5]Pathology Department, Hospital Universitario 12 de Octubre, Madrid, Spain; [6]Pathology Department, Hospital MD Anderson Cancer Center, Madrid, Spain; [7]Pathology Department, Hospital Virgen de la Salud, Toledo, Spain; [8]Pathology Department, Hospital Universitario Ramón y Cajal, Madrid, Spain; [9]Pathology Department, Hospital Universitario Puerta de Hierro-Segovia de Arana, Madrid, Spain; [10]Pathology Department, Hospital Universitari de Bellvitge, IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain; [11]Haematology Department, Hospitalario Universitario de Salamanca (HUS/IBSAL), Salamanca, Spain; [12]Bioinformatics Unit, Instituto de Investigación Sanitaria-Fundación Jiménez Díaz University Hospital, Universidad Autónoma de Madrid (IIS-FJD, UAM), Madrid, Spain; [13]Department of Genetics, Instituto de Investigación Sanitaria-Fundación Jiménez Díaz University Hospital, Universidad Autónoma de Madrid (IIS-FJD, UAM), Madrid, Spain; [14]Center for Biomedical Network Research on Rare Diseases (CIBERER), ISCIII, Madrid, Spain; [15]Kura Oncology Inc., San Diego, CA; and [16]UGC Laboratorios, Hospital Universitario de Puerto Real, Cádiz, Spain

Key Points

- Gene expression and mutational analysis confirm the differences among the 3 peripheral TCL subclasses: AITL, PTCL-NOS, and PTCL-TFH.
- The expression of a gene set, including B-cell genes, is an IPI-independent prognostic factor for AITL cases.

Peripheral T-cell lymphoma (PTCL) is a clinically aggressive disease, with a poor response to therapy and a low overall survival rate of approximately 30% after 5 years. We have analyzed a series of 105 cases with a diagnosis of PTCL using a customized NanoString platform (NanoString Technologies, Seattle, WA) that includes 208 genes associated with T-cell differentiation, oncogenes and tumor suppressor genes, deregulated pathways, and stromal cell subpopulations. A comparative analysis of the various histological types of PTCL (angioimmunoblastic T-cell lymphoma [AITL]; PTCL with T follicular helper [TFH] phenotype; PTCL not otherwise specified [NOS]) showed that specific sets of genes were associated with each of the diagnoses. These included TFH markers, cytotoxic markers, and genes whose expression was a surrogate for specific cellular subpopulations, including follicular dendritic cells, mast cells, and genes belonging to precise survival (NF-κB) and other pathways. Furthermore, the mutational profile was analyzed using a custom panel that targeted 62 genes in 76 cases distributed in AITL, PTCL-TFH, and PTCL-NOS. The main differences among the 3 nodal PTCL classes involved the $RHOA^{G17V}$ mutations ($P < .0001$), which were approximately twice as frequent in AITL (34.09%) as in PTCL-TFH (16.66%) cases but were not detected in PTCL-NOS. A multivariate analysis identified gene sets that allowed the series of cases to be stratified into different risk groups. This study supports and validates the current division of PTCL into these 3 categories, identifies sets of markers that can be used for a more precise diagnosis, and recognizes the expression of B-cell genes as an IPI-independent prognostic factor for AITL.

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*M.R., R.A.-A., and L.T.-R. contributed equally to this article.

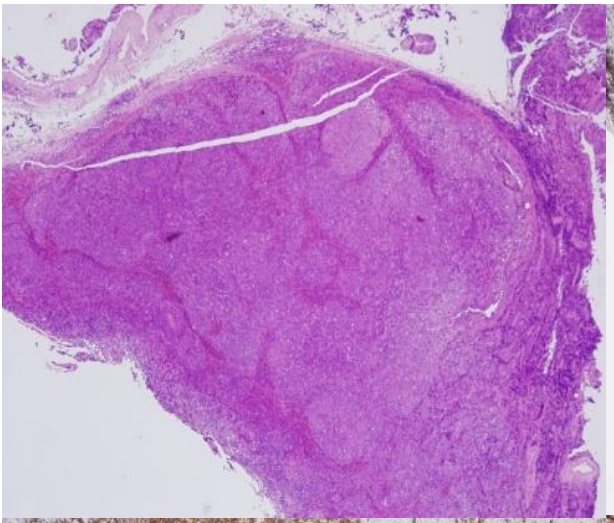
The microarray data have been deposited in BioProject (accession number PRJNA752277); https://www.ncbi.nlm.nih.gov/bioproject/752277.

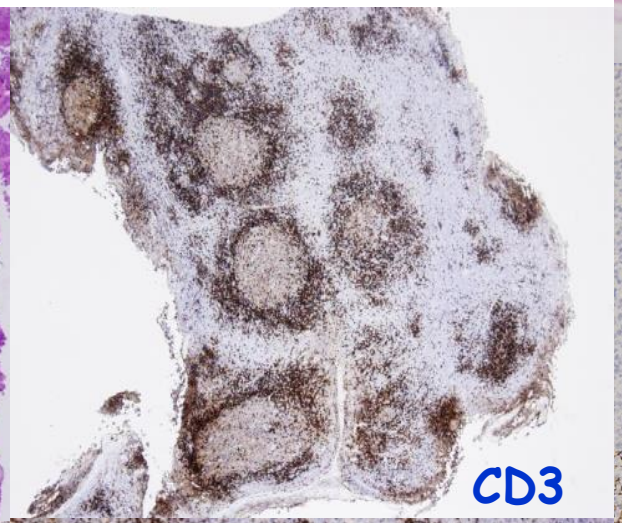
Data associated with this study are available upon request by emailing marta.rodriguezm@quironsalud.es.

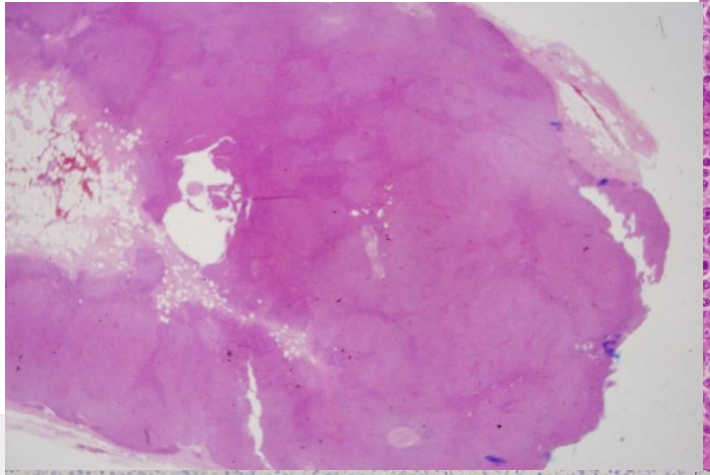
The full-text version of this article contains a data supplement.

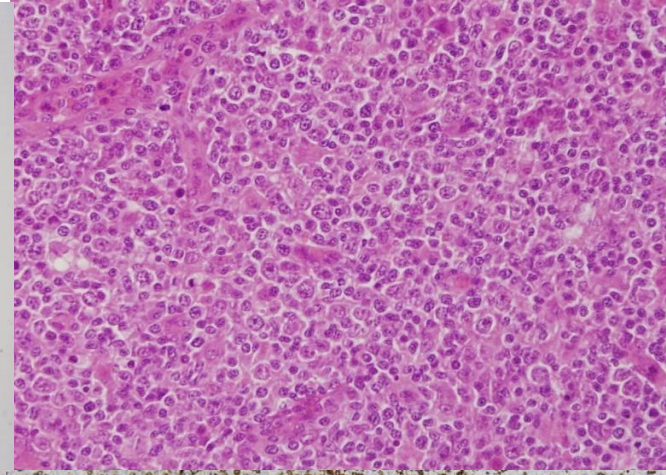
AITL

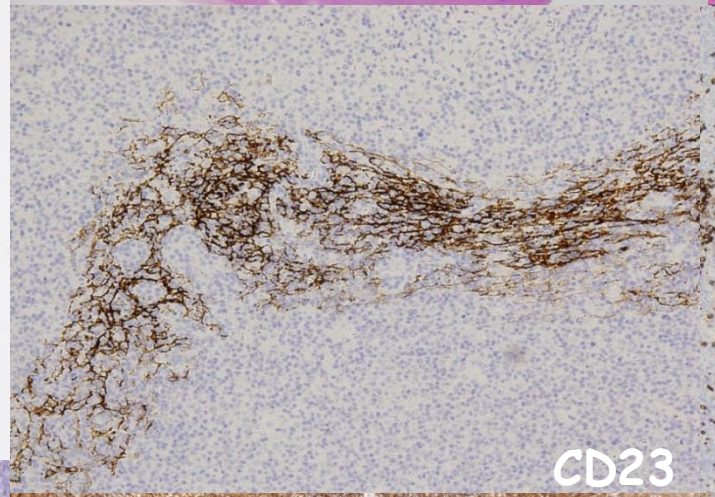
Attygalle AD, et al. Am J Surg Pathol, 2007

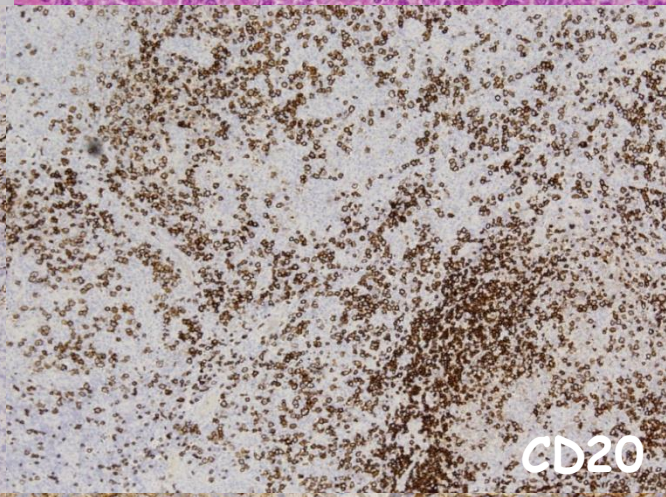


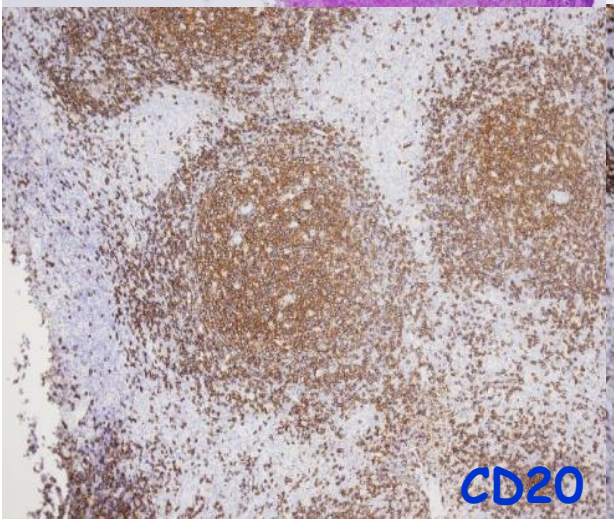


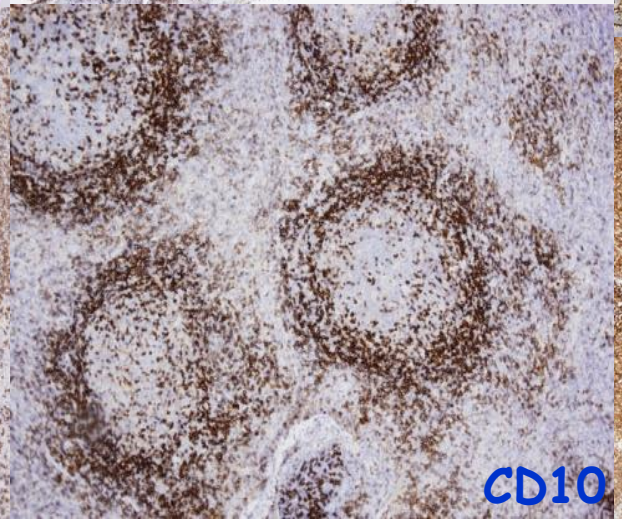


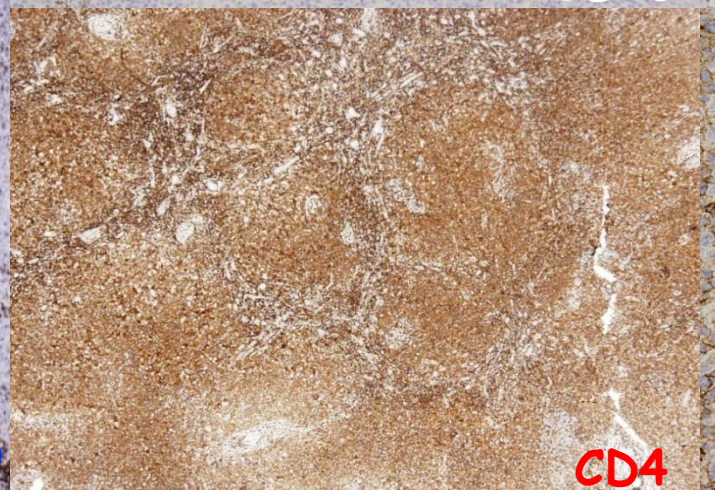


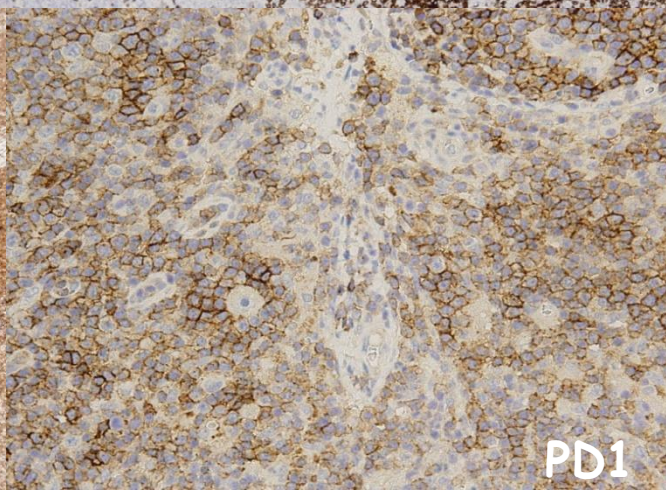




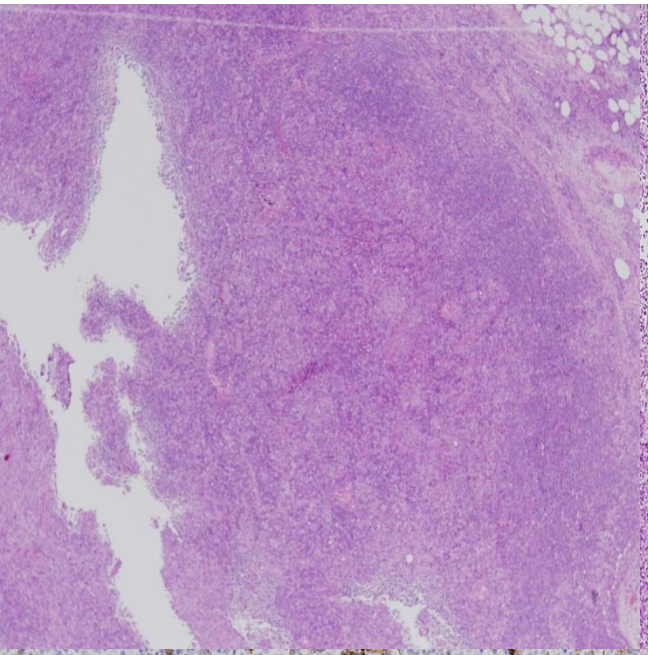


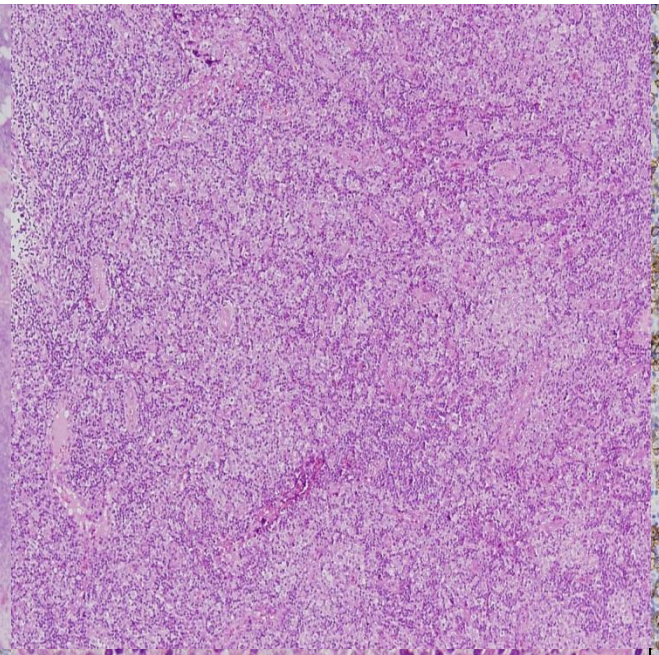


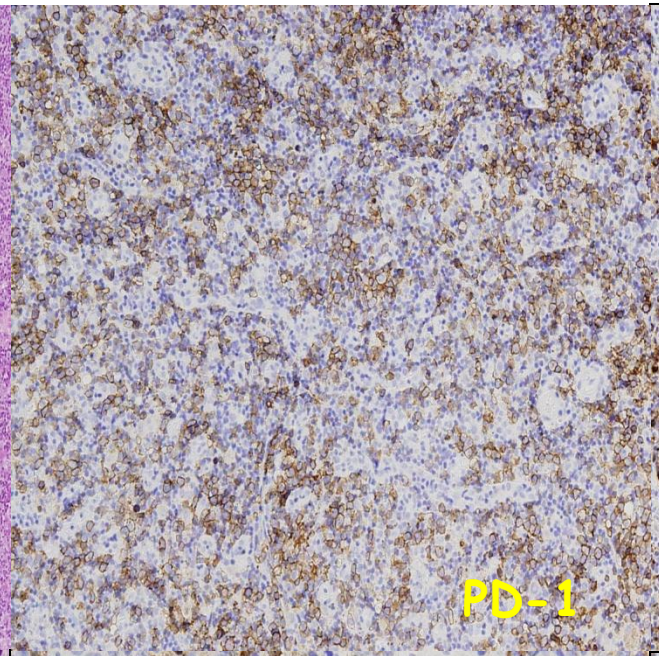


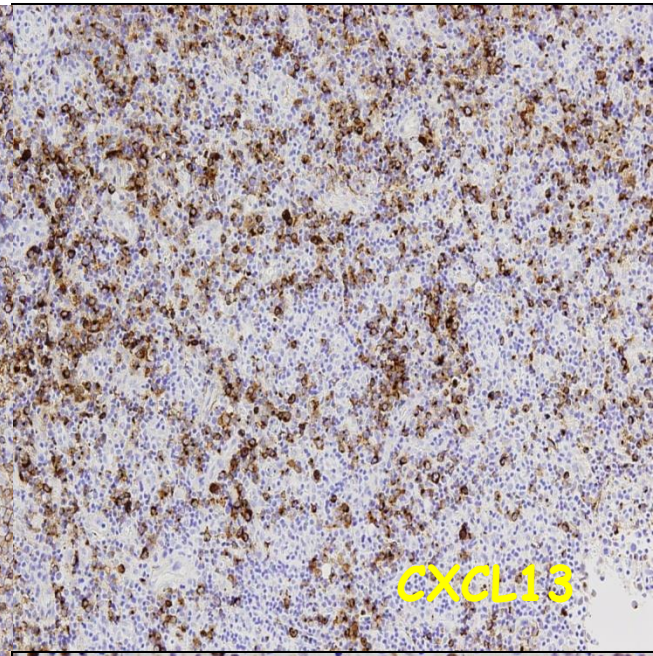


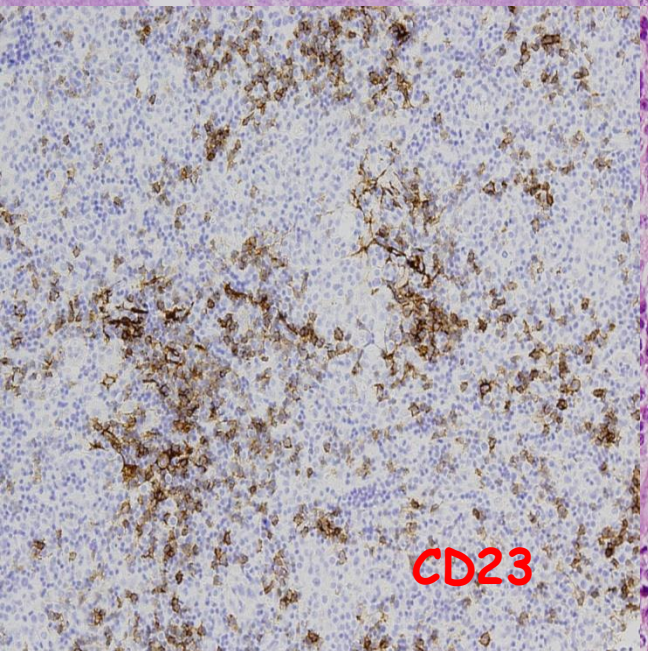
PTCL-NOS-TFH

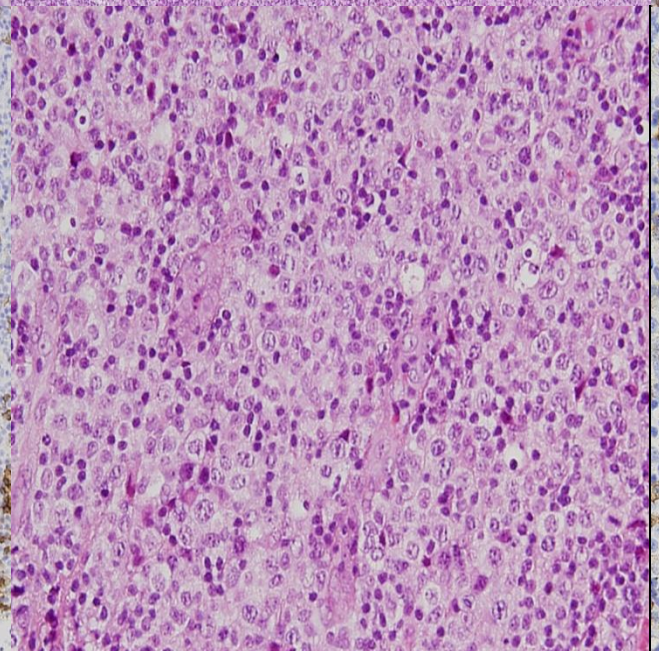


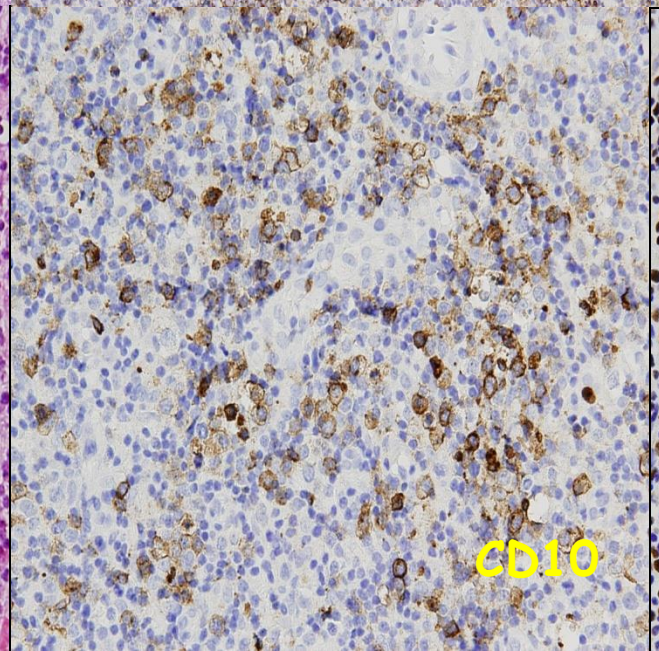


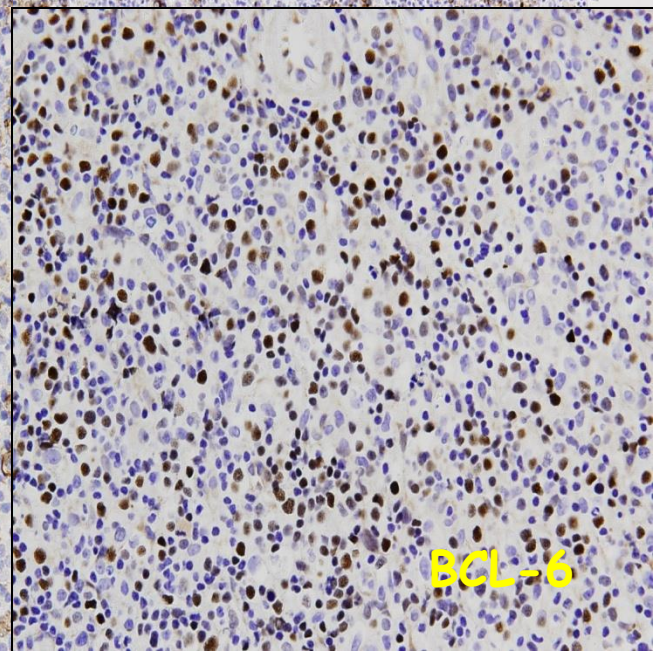




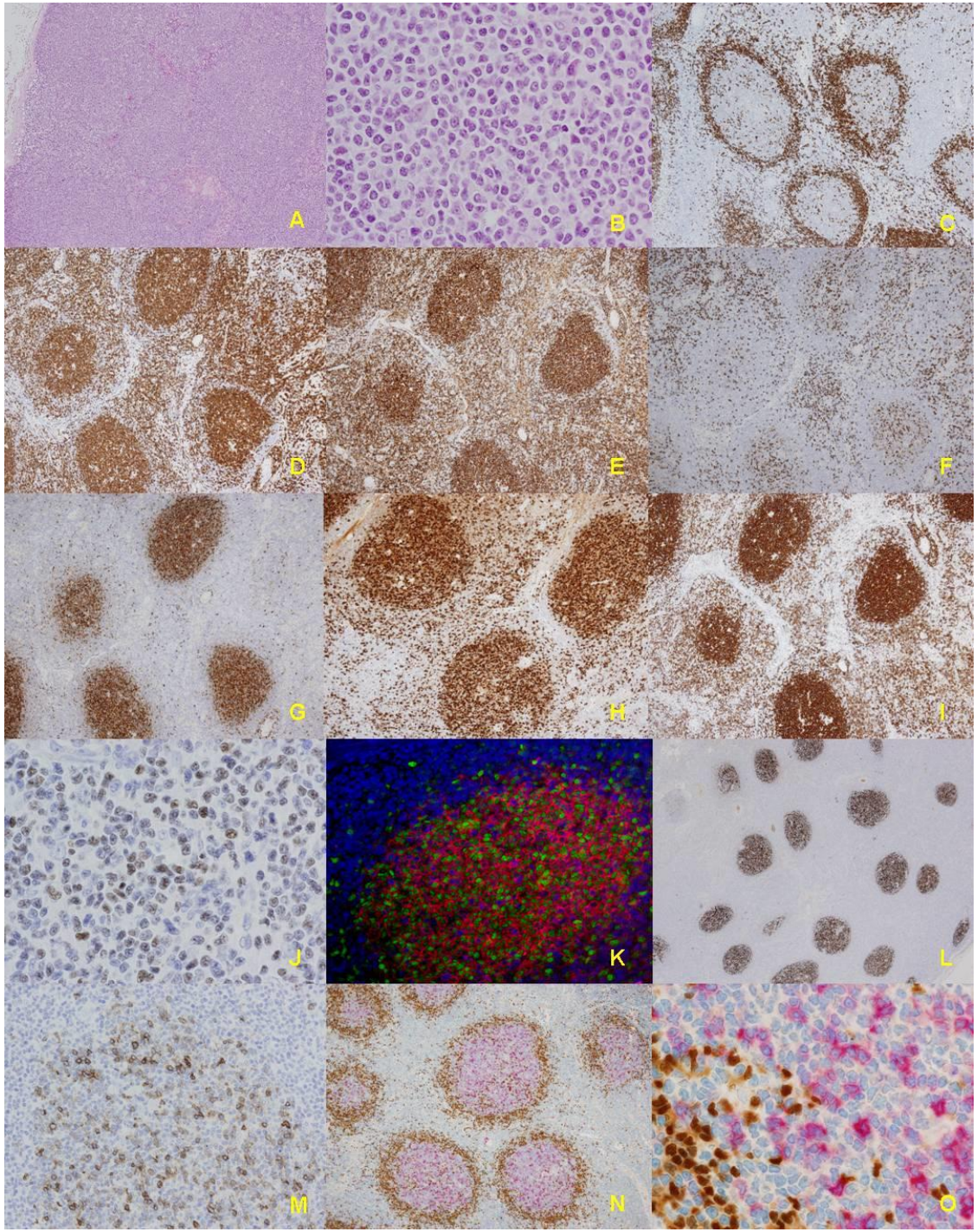


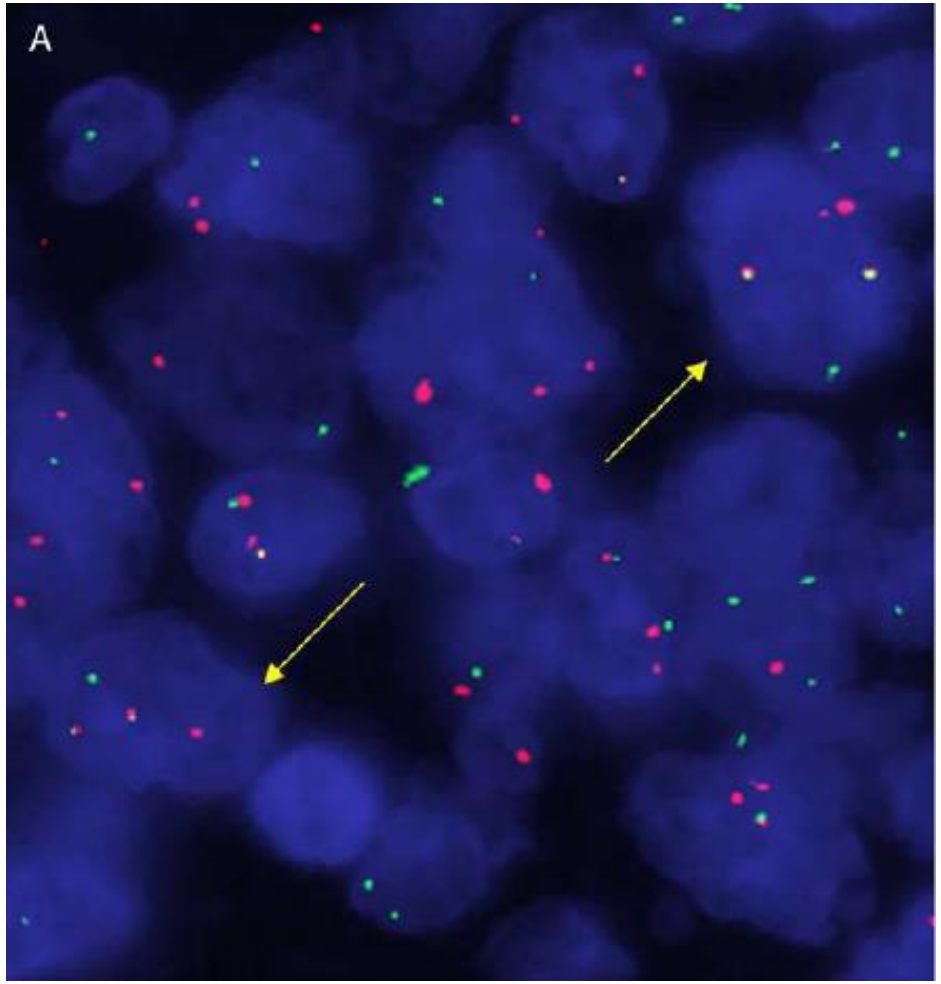






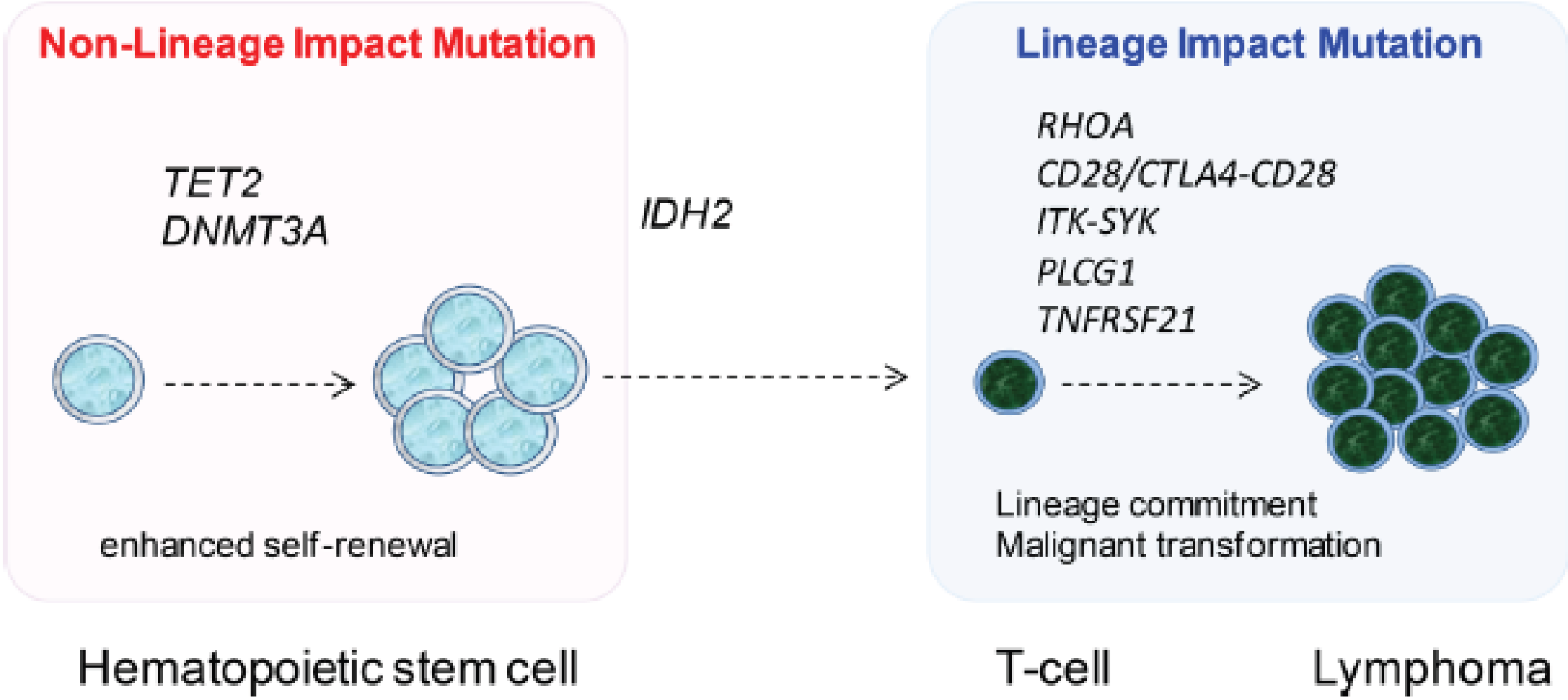
FOLLICULAR T-CELL LYMPHOMA



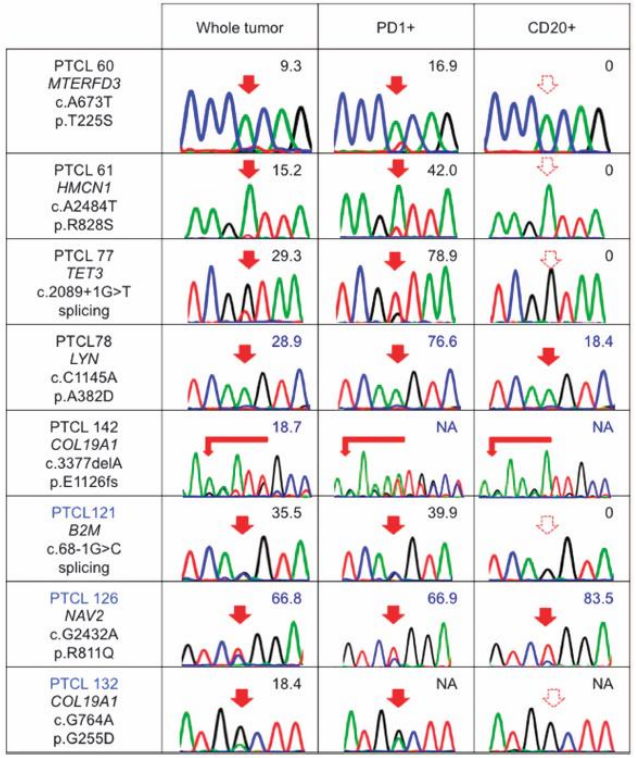


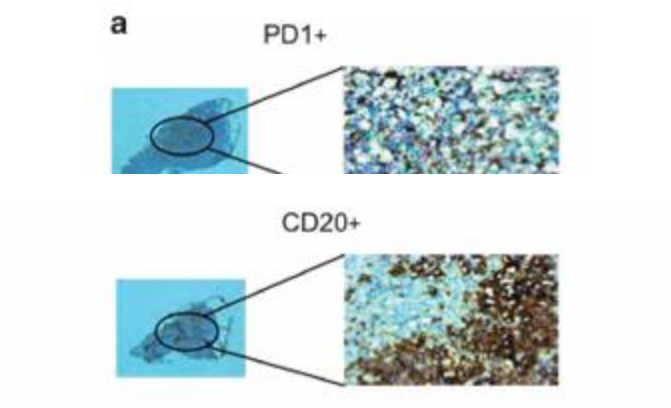
ITK/SYK fusión ; t(5;9)(q33;q22)

Wang M , et al; Oncotarget, 2017



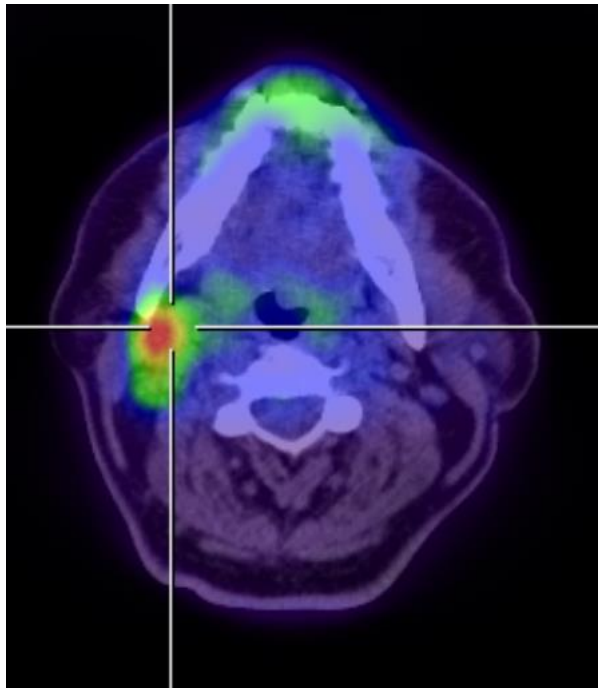
Nguyen TB, et al; Blood Cancer Journal, 2017

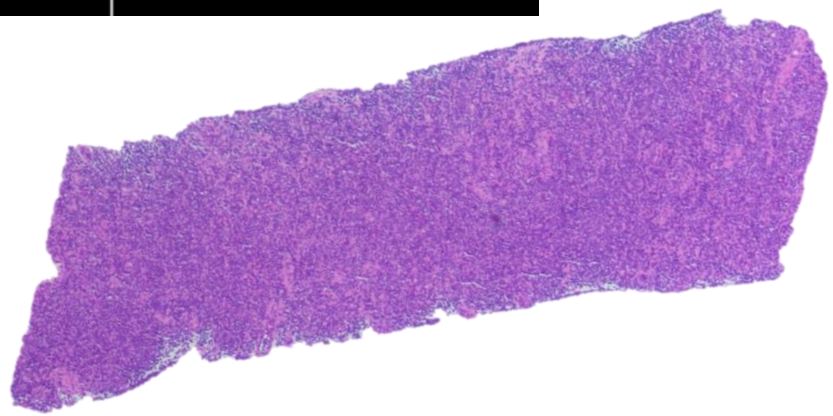




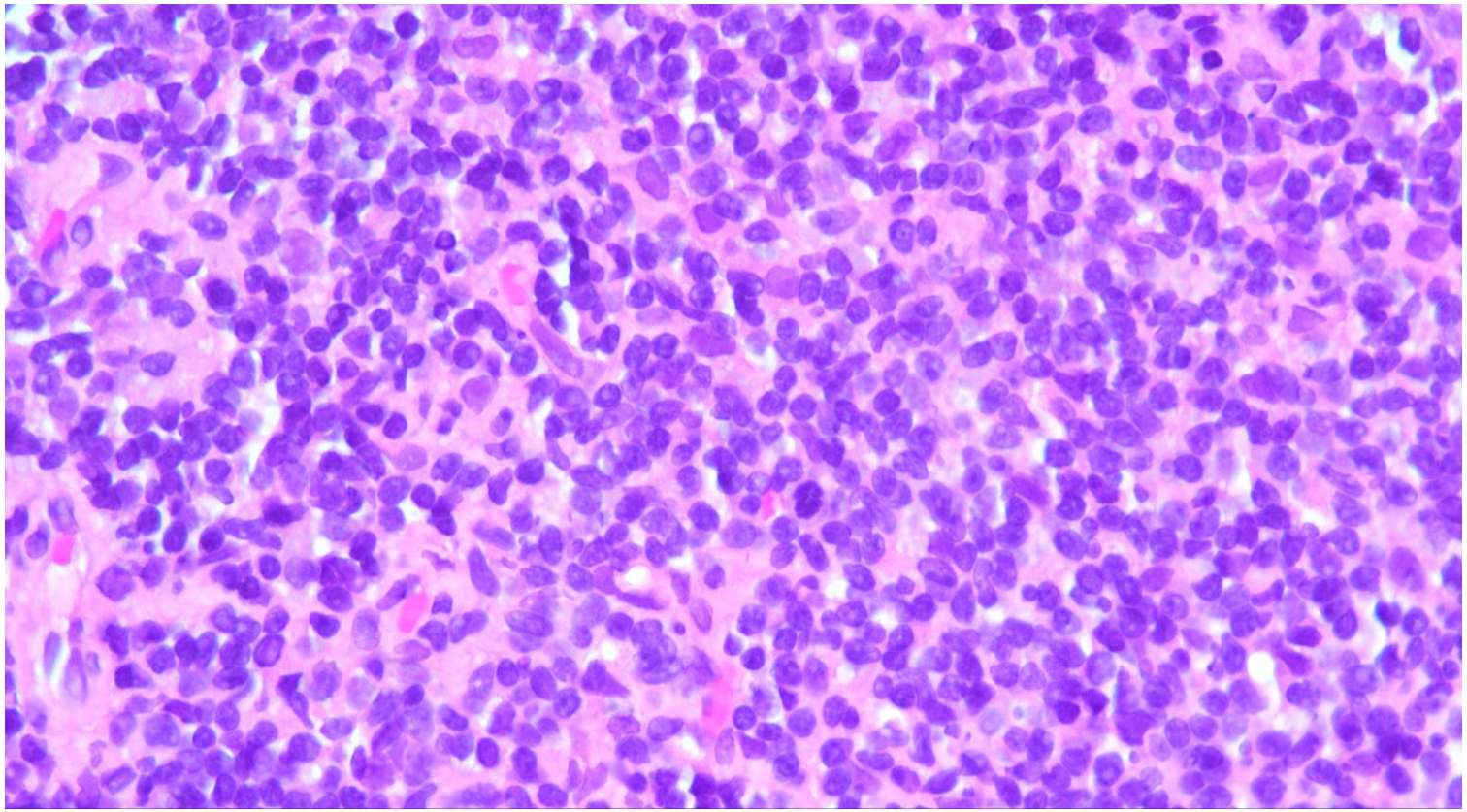
	TET2			DNMT3A			RHOA			IDH2			NOTCH1			IgH VDJ status
	whole tumor	PD1+	CD20+	whole tumor	PD1+	CD20+	whole tumor	PD1+	CD20+	whole tumor	PD1+	CD20+	whole tumor	PD1+	CD20+	
PTCL2	1.5	86.6	4.9	30.6	22.2	41.5	15.5	51.8								
	29.5	16.6	24.9													
PTCL8	6.8	51.4	28.7	5.6	27.9		4.9	23.1		5.5	22.7					
	5.8	20.2														
PTCL60	10.0	36.4	47.5	11.5	48.6	6.2										
	12.6	30.9														
PTCL61	42.1	27.8	36.1				10.7	34.4		9.1	26.9					
PTCL63	17.1	29.1	11.7				13.8	16.9		12.2	15.6		17.4		100	OC
	21.0	60.1	45.1													
PTCL70	30.6	31.6	45.1	35.7	14.7		9.6	66.0		8.2	30.3					
PTCL74				2.4	27.9								22.4		100	MC
PTCL77	13.8	41.6	24.8				14.0	49.9								
	16.8	59.9														
PTCL78	54.5	79.7					39.4	41.1					23.7		40.3	OC
PTCL80	32.5	73.3	100													
PTCL136	28.0	23.9	44.9	41.3	56.9	15.7	13.4	28.2								
	37.8	34.9	21.8													
PTCL142	20.2	27.3	54.5				22.8	48.6								
PTCL144	34.7	26.3	51.0													
PTCL121	27.7	44.1	37.7													
	36.2	50.0														
PTCL123	Pos	Pos	Pos													
	9.1	25.8														
PTCL127	Pos	Pos	Pos	32.0	55.7	25.4	30.4	28.6								
	Pos	Pos	Pos													
PTCL129	24.4	59.5	15.7													
	Pos	Pos	Pos													

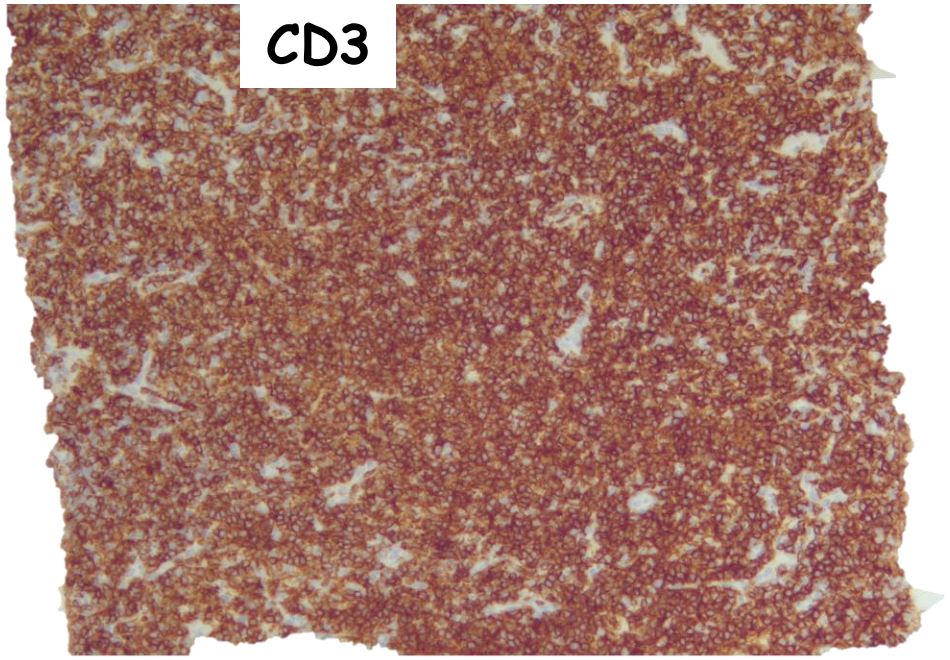
Noviembre 2008	Diciembre 2018	

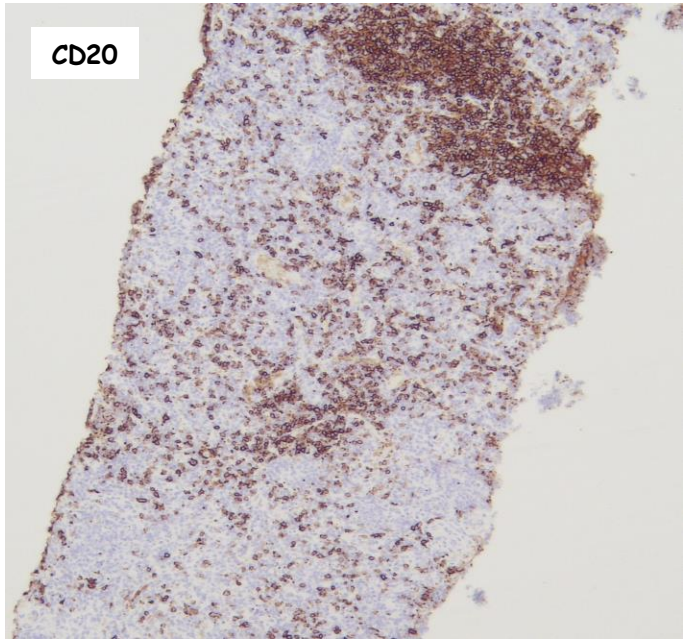




Recaída de LINFOMA DE CÉLULAS T ANGIOINMUNOBLÁSTICO




CD3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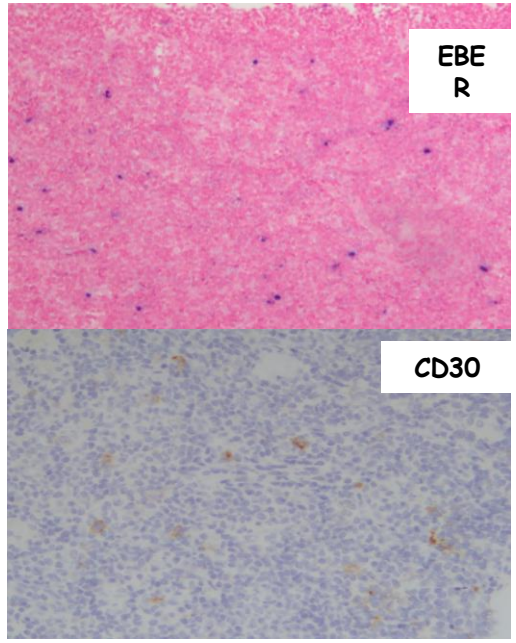
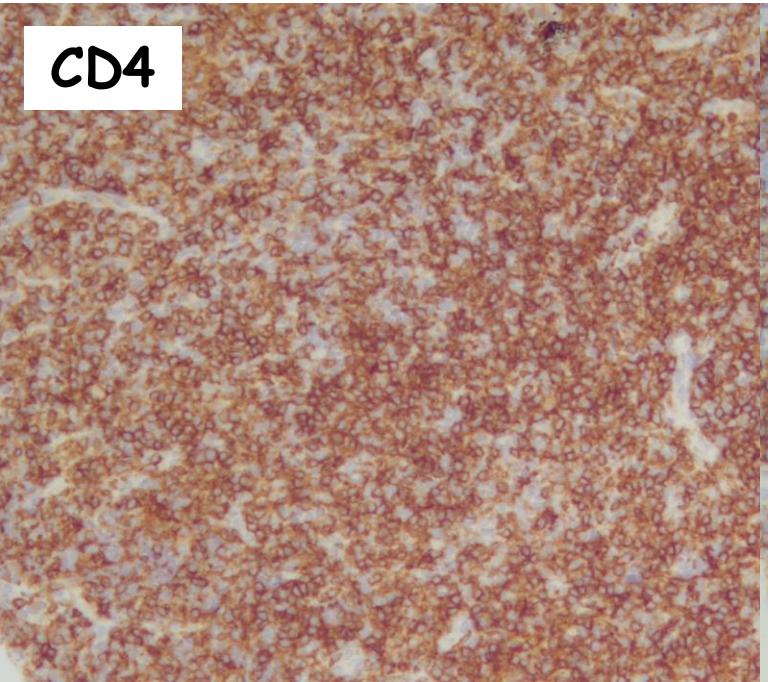

EBE
R
CD30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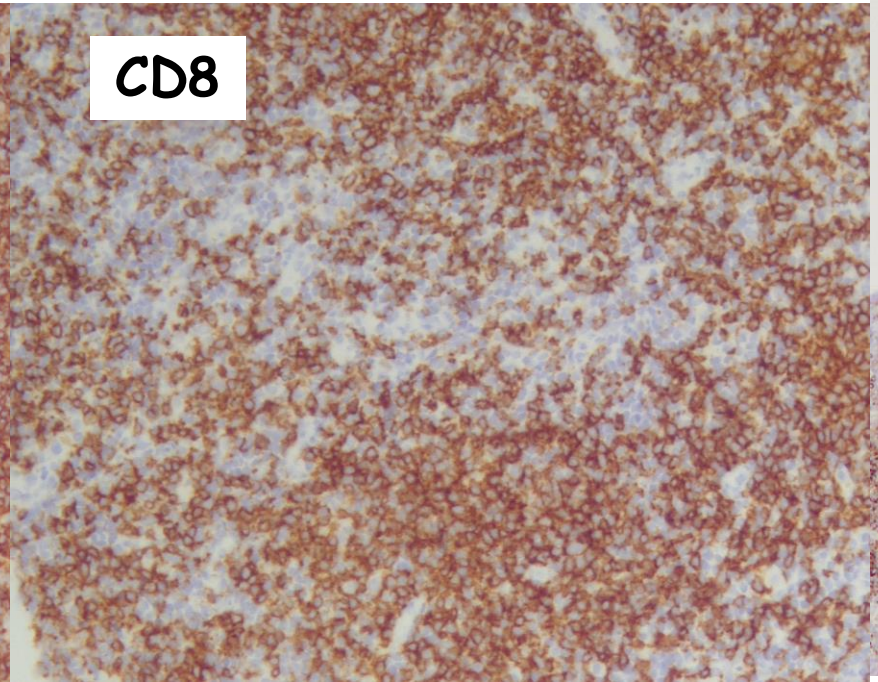
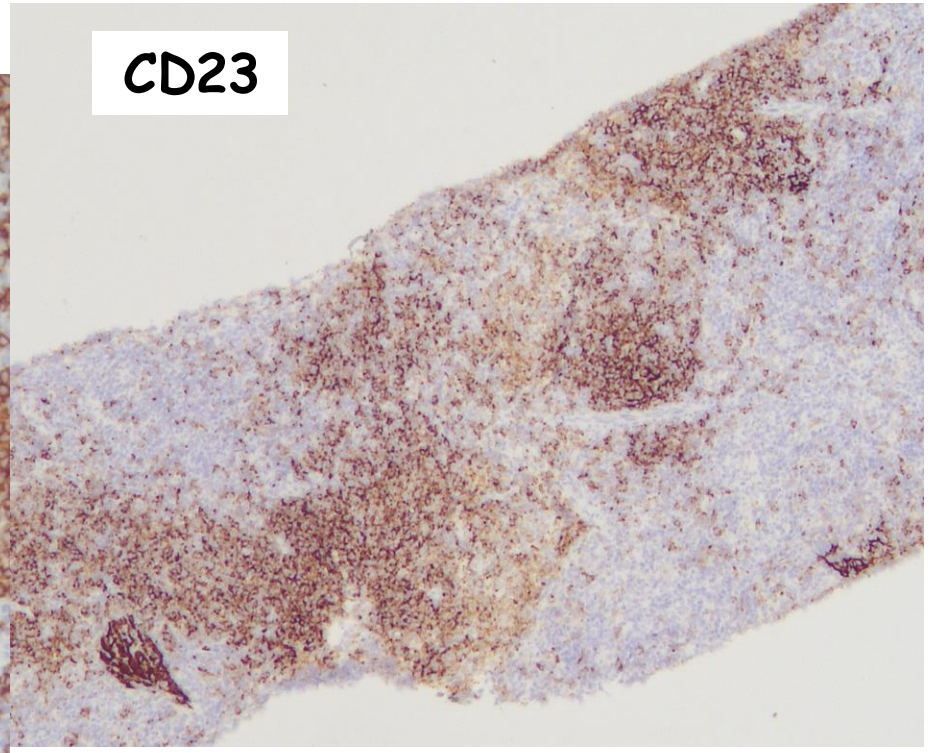
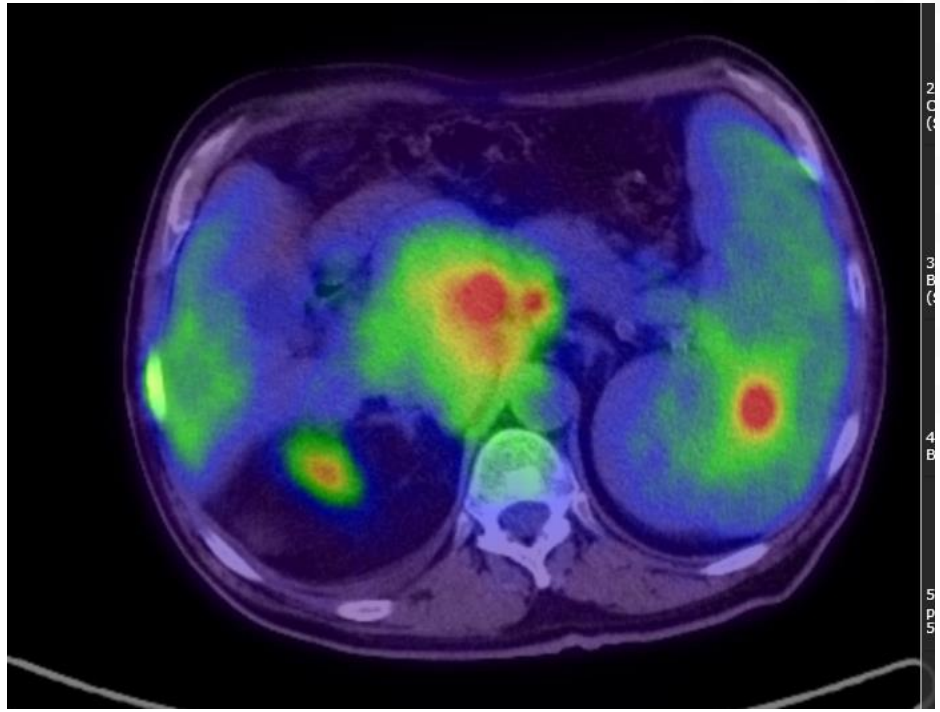

CD8


CD23

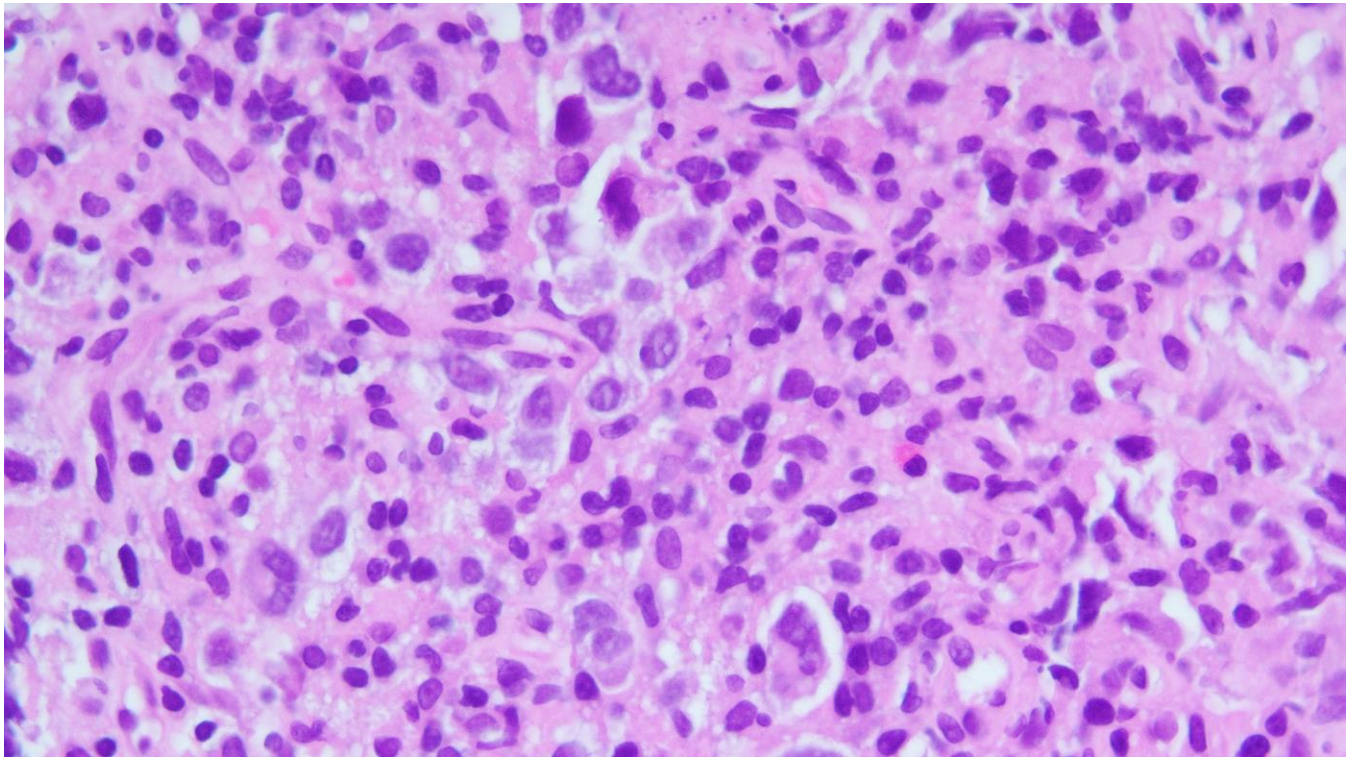
HISTORIA CLÍNICA 2022

Noviembre 2008	Diciembre 2018	Abril 2022

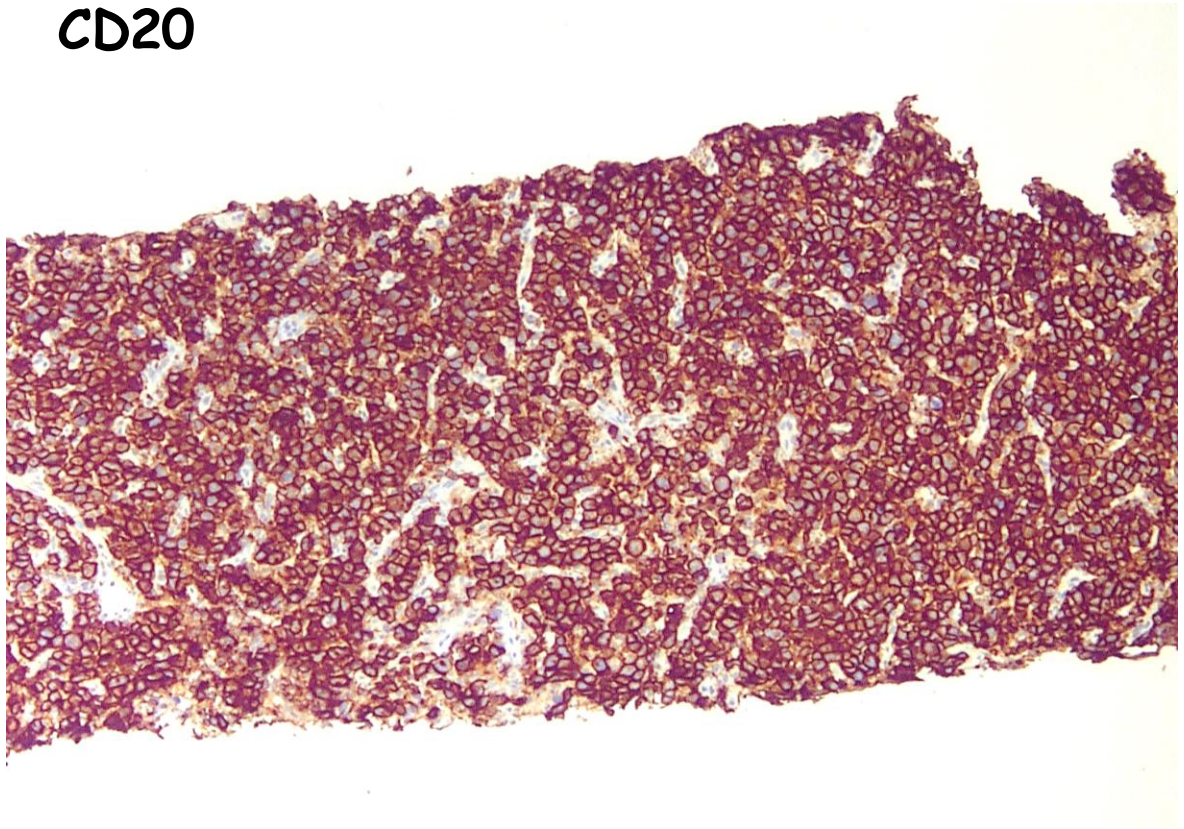


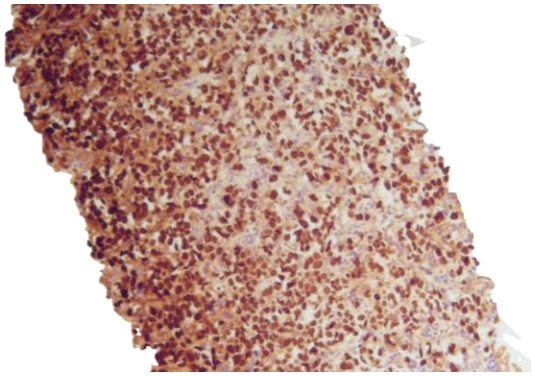
- Paciente varón 75 años:
  - Linfoma T angioinmunoblástico en **2008**, tratado con GIFOX x4. No TMO
  - Recaída tardía en **2018**, tratado con CHOEP x3 + mini CHOP x1. SLP: 3 años
  - Abril **2022**: Cuadro constitucional y LDH: 431 U/L
- PET-TAC:

Adenopatías supra e infradiafragmáticas, esplenomegalia, LOE hepática y lesiones óseas

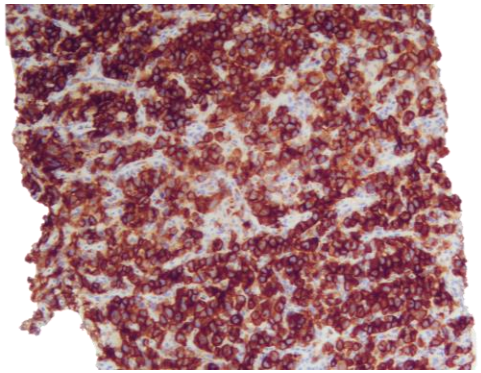


CD20





EBER



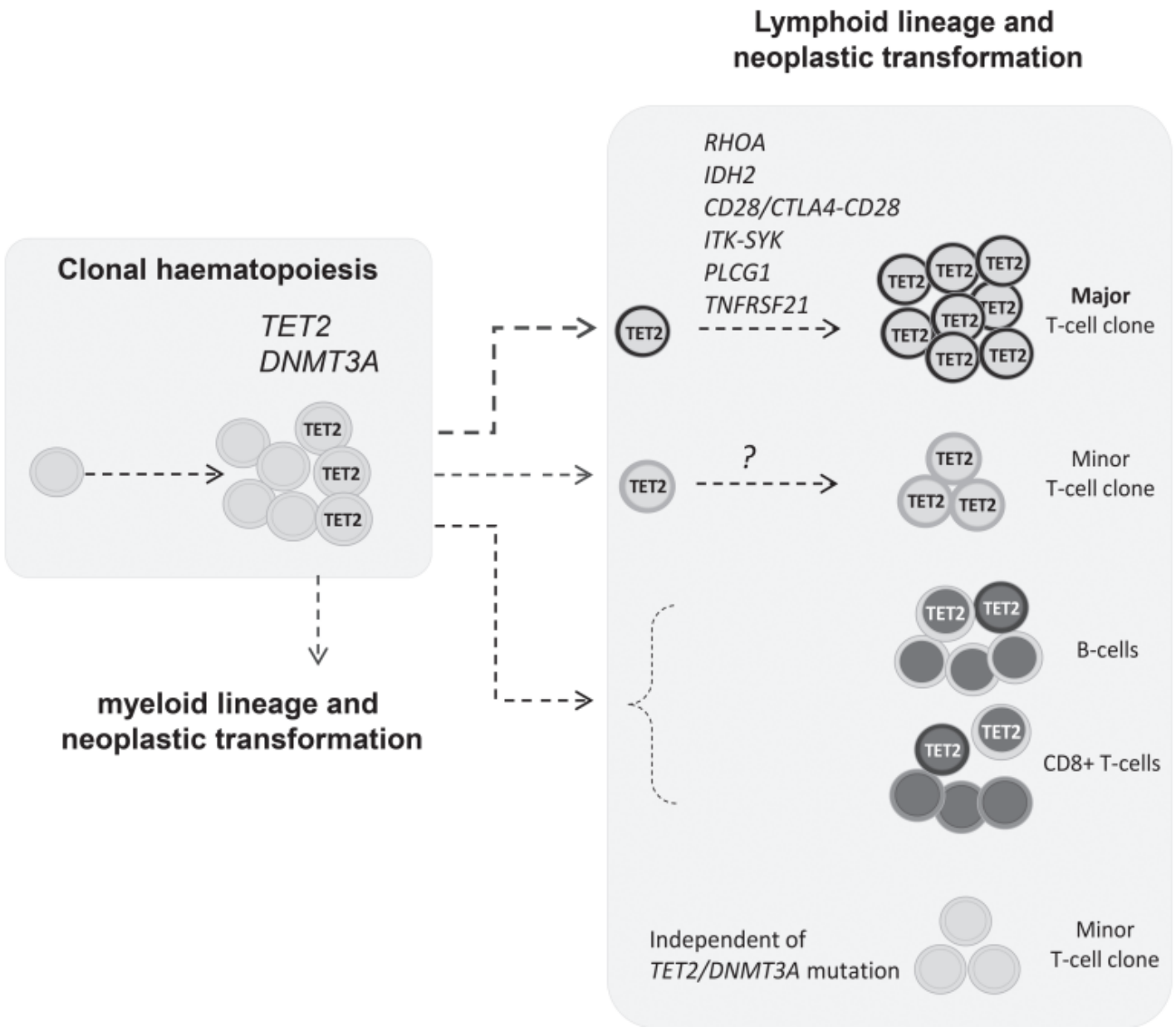
CD30

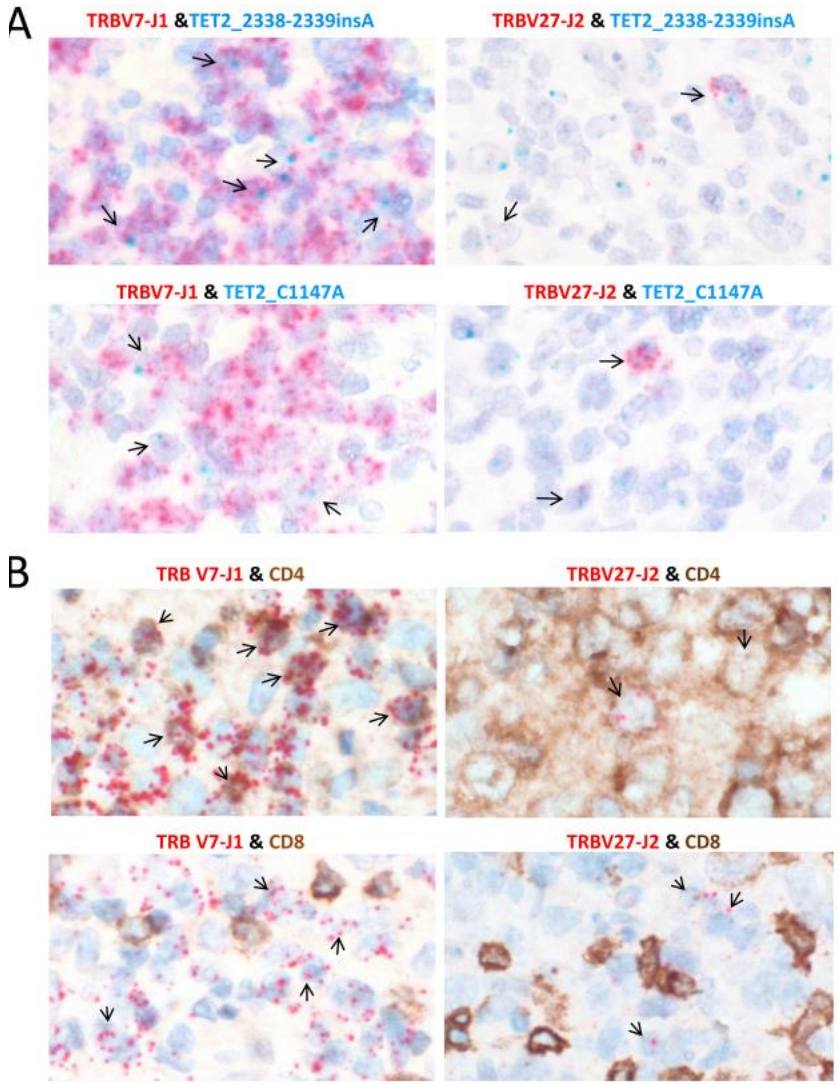
nº biopsia	NGS [Panel investigación LT, Magnis]
LINFOMA T ANGIOINMUNOBLASTICO	RHOA-G17V (PROBABLEMENTE PATOGENICA, 14%)
	TET2-G355D (VUS, 47%)
	TET2-V698Cfs*2 (P.PATOG, 16%)
	TET2-N1843Kfs*44 (P.PATOG, 16%)
	JAK1-R532H (VUS, 44%)
LINFOMA B DIFUSO DE CELULAS GRANDES EBV-POSITIVO	TET2-G355D (VUS, 47%)
	TET2-V698Cfs*2 (P.PATOG, 16%)
	TET2-N1843Kfs*44 (P.PATOG, 16%)
	JAK1-R532H (VUS, 44%)
	TP53-R248W (PATOG, 9%)

Estudio en una serie de 12 pacientes

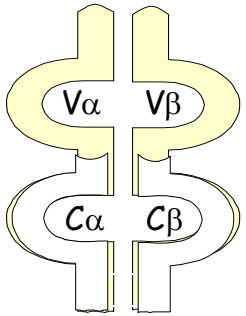
Bi-clonal T-cell populations from a *TET2* mutant progenitor

Wen-Qing Yao, et al. J Pathol, 2020





T-Cell Neoplasms



TCR

TCR alpha rearrangement

TCR beta rearrangement

TCR gamma rearrangement

TCR delta rearrangement | TCR delta deletion

CD3 TdT — CD4 — CD7 CD5 CD2 CD3 — CD8 — CD3 TdT — Mature thymocyte

CD4 — CD7 CD5 CD2 CD3 — CD8 — Mature T-cell

TH cells

TS cells

TdT	CD3 TdT	CD3 TdT	CD3 TdT
Lymphoid precursor cell	Pro-thymocyte	Inmature thymocyte	Common thymocyte
HLA-DR CD34	HLA-DR CD34 CD7 CD2	CD7 CD2 CD5	CD7 CD2 CD5 CD1 CD4/CD8
BONE MARROW		THYMUS (cortex)	

Mature thymocyte	Mature T-cell
THYMUS (medula)	Peripheral blood Lymphoid tissues

Estancia:
Queen's University Belfast, Health Sciences Building
Belfast. Irlanda del Norte.UK

21 pacientes AITL, al menos 2 muestras (media 2, 2-4))

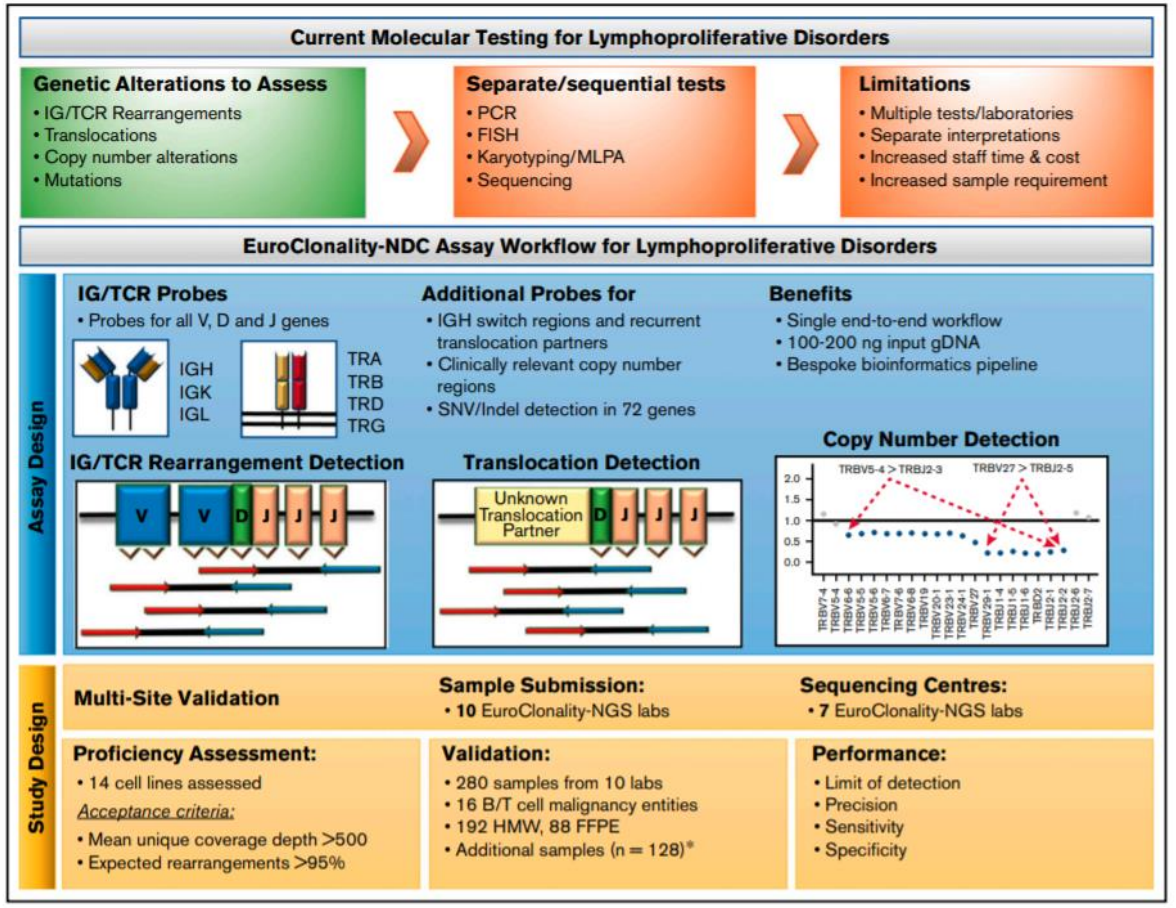


Figure 1. Current molecular testing workflow and EuroClonality-NDC workflow for LPDs. Genetic alterations required to be tested (green box) can be performed

REGULAR ARTICLE

blood advances

Check for updates

Validation of the EuroClonality-NGS DNA capture panel as an integrated genomic tool for lymphoproliferative disorders

James Peter Stewart,[1] Jana Gazdova,[1] Nikos Darzentas,[2] Dörte Wren,[3] Paula Proszek,[3] Grazia Fazio,[4] Simona Songia,[4] Miguel Alcoceba,[5-7] Maria Eugenia Sarasquete,[5-7] Patrick Villarese,[8] Michèle Y. van der Klift,[9] Kim C. Heezen,[9] Neil McCafferty,[1] Karol Pal,[2] Mark Catherwood,[10] Chang Sik Kim,[1] Shambhavi Srivastava,[1] Leonie I. Kroeze,[11] Elizabeth Hodges,[1] Kostas Stamatopoulos,[12] Wolfram Klapper,[13] Elisa Genuardi,[14] Simone Ferrero,[14] Michiel van den Brand,[11] Giovanni Cazzaniga,[4] Frederic Davi,[15] Lesley-Ann Sutton,[16] Ramon Garcia-Sanz,[5-7] Patricia J. T. A. Groenen,[11] Elizabeth A. Macintyre,[8] Monika Brüggemann,[2] Christiane Pott,[2] Anton W. Langerak,[9,*] and David Gonzalez,[1,*] on behalf of the EuroClonality-NGS Working Group

Key Points

- NGS validated for simultaneous detection of IG/TCR rearrangements, translocations, CNAs, and single-nucleotide variants/indels.
- Accompanying bioinformatic pipelines enable automated objective reporting of immunogenetic and oncogenetic alterations.

RESULTADOS

Patient Number	IGH	IGK	IGL	TRA	TRB	TRD	TRG
1	NC	NC	NC	C	NC	NC	C
2	NC	NC	NC	NC	NC	NC	C
3	NC	NC	NC	C	C	NC	C
4	NC	C	NC	C	NC	NC	C
5	NC	C	NC	C	C	NC	C
6	C	NC	NC	C	C	NC	C
7	NC	NC	NC	C	C	NC	C
8	C	NC	NC	C	C	NC	C
9	C	C	C	NC	NC	NC	C
10	NC	NC	NC	C	C	NC	C
11	NC	NC	NC	C	C	NC	C
12	C	NC	NC	C	C	NC	C
13	C	NC	NC	C	C	NC	C
14	NC	C	NC	C	C	NC	C
15	NC	NC	NC	C	C	NC	C
16	NC	NC	NC	C	C	NC	C
17	NC	NC	NC	C	C	NC	C
18	NC	NC	NC	C	C	NC	C
19	NC	NC	NC	C	C	NC	C
20	NC	NC	NC	C	C	NC	C
21	NC	NC	NC	NC	NC	NC	C

TCRG_CLONAL_100%
TCRB_CLONAL_76.2 (16/21)
TCRA_CLONAL_85.7% (18/21)
TCRD_CLONAL_ 0%

IGH_CLONAL_23.8% (5/21)
IGK_CLONAL_28.6% (6/21)
IGL_CLONAL_4.8 %(1/21)

Al menos uno clonal _42.9% (9/21)

Patient Number	Sampling Order	TRA Rearrangements		TRB Rearrangements		TRG Rearrangements	
1	1	TRAJ52>TRAV12-2	TRAJ53>TRAV26-2	no clonal rr	no clonal rr	TRGJ2>TRGV2	TRGJ2>TRGV4
1	2	TRAJ52>TRAV12-2	TRAJ53>TRAV26-2	no clonal rr	no clonal rr	TRGJ2>TRGV2	TRGJ2>TRGV4
2	1	TRAJ20>TRAV8-3	TRAJ5>TRAV12-1	no clonal rr	no clonal rr	TRGJ2>TRGV10	TRGJ2>TRGV2
2	2	TRAJ20>TRAV8-3	TRAJ5>TRAV12-1	no clonal rr	no clonal rr	TRGJ2>TRGV10	TRGJ2>TRGV2
2	3	TRAJ20>TRAV8-3	TRAJ5>TRAV12-1	no clonal rr	no clonal rr	TRGJ2>TRGV10	TRGJ2>TRGV2
3	1	TRAJ40>TRAV25	TRAJ45>TRAV13-1	TRBJ2-7>TRBV28	TRBJ2-4>TRBV27	TRGJ2>TRGV8	TRGJ2>TRGV9
3	2	TRAJ40>TRAV25	TRAJ45>TRAV13-1	TRBJ2-7>TRBV28	TRBJ2-4>TRBV27	TRGJ2>TRGV8	TRGJ2>TRGV9
4	1	TRAJ42>TRAV35	TRAJ61>TRAV38-2/DV8	no clonal rr	no clonal rr	TRGJP1>TRGV8	TRGJ2>TRGV5
4	2	TRAJ42>TRAV35	TRAJ61>TRAV38-2/DV8	no clonal rr	no clonal rr	TRGJP1>TRGV8	TRGJ2>TRGV5
5	1	TRAJ45>TRAV29/DV5	no clonal rr	TRBJ2-7>TRBV5-1	TRBJ2-4>TRBD1	TRGJ2>TRGV10	TRGJ2>TRGV4
5	2	TRAJ45>TRAV29/DV5	no clonal rr	TRBJ2-7>TRBV5-1	TRBJ2-4>TRBD1	TRGJ2>TRGV10	TRGJ2>TRGV4
5	3	TRAJ45>TRAV29/DV5	no clonal rr	TRBJ2-7>TRBV5-1	TRBJ2-4>TRBD1	TRGJ2>TRGV10	TRGJ2>TRGV4
6	1	TRAJ54>TRAV38-1	TRAJ47>TRAV26-1	TRBD2>TRBV2	TRBJ2-3>TRBVD2	TRGJ2>TRGV3	TRGJ2>TRGV4
6	2	TRAJ54>TRAV38-1	TRAJ47>TRAV26-1	TRBD2>TRBV2	TRBJ2-3>TRBVD2	TRGJ2>TRGV3	TRGJ2>TRGV4
7	1	TRAJ20>TRAV8-3	TRAJ10>TRAV23/DV6	TRBJ1-6>TRBV3-1	TRBJ1-1>TRBD1	TRGJ2>TRGV8	TRGJ2>TRGV3
8	1	TRAJ42>TRAV9-2	TRAJ7>TRAV29/DV5	TRBJ2-7>TRBV20-1	TRBJ2-5>TRBD2	TRGJ2>TRGV9	no clonal rr
8	2	TRAJ42>TRAV9-2	TRAJ7>TRAV29/DV5	TRBJ2-7>TRBV20-1	TRBJ2-5>TRBD2	TRGJ2>TRGV9	no clonal rr
8	3	TRAJ42>TRAV9-2	TRAJ7>TRAV29/DV5	TRBJ2-7>TRBV20-1	TRBJ2-5>TRBD2	TRGJ2>TRGV9	no clonal rr
8	4	TRAJ42>TRAV9-2	TRAJ7>TRAV29/DV5	TRBJ2-7>TRBV20-1	TRBJ2-5>TRBD2	TRGJ2>TRGV9	no clonal rr
9	1	TRAJ21>TRAV9-2	TRAJ41>TRAV25	TRBJ1-1>TRBV18	TRBD2>TRBD1	TRGJ1>TRGV4	TRGJP1>TRGV8
9	2	TRAJ21>TRAV9-2	TRAJ41>TRAV25	TRBJ1-1>TRBV18	TRBD2>TRBD1	TRGJ1>TRGV4	TRGJP1>TRGV8
9	3	TRAJ21>TRAV9-2	TRAJ41>TRAV25	TRBJ1-1>TRBV18	TRBD2>TRBD1	TRGJ1>TRGV4	TRGJP1>TRGV8
10	1	TRAJ13>TRAV8-6	TRAJ17>TRAV10	TRBJ1-2>TRBV19	TRBJ2-3>TRBV6-5	TRGJP>TRGV9	TRGJ2>TRGV8
10	2	TRAJ13>TRAV8-6	TRAJ17>TRAV10	TRBJ1-2>TRBV19	TRBJ2-3>TRBV6-5	TRGJP>TRGV9	TRGJ2>TRGV8
11	1	TRAJ17>TRAV23/DV6	TRAJ57>TRAV29/DV5	TRBJ1-2>TRBD1	TRBJ2-7>TRBD2	TRGJ2>TRGV3	TRGJP2>TRGV8
11	2	TRAJ17>TRAV23/DV6	TRAJ57>TRAV29/DV5	TRBJ1-2>TRBD1	TRBJ2-7>TRBD2	TRGJ2>TRGV3	TRGJP2>TRGV8
12	1	TRAJ31>TRAV41	TRAJ53>TRAV25	TRBJ1-2>TRBV5-1	TRBJ2-2>TRBD2	TRGJ2>TRGV10	TRGJP2>TRGV8
12	2	TRAJ31>TRAV41	TRAJ53>TRAV25	TRBJ1-2>TRBV5-1	TRBJ2-2>TRBD2	TRGJ2>TRGV10	TRGJP2>TRGV8
13	1	TRAJ36>TRAV8-6	TRAJ37>TRAV27	TRBJ2-7>TRBD2	TRBJ2-5>TRBV20-1	TRGJ2>TRGV8	no clonal rr
13	2	TRAJ36>TRAV8-6	TRAJ37>TRAV27	TRBJ2-7>TRBD2	TRBJ2-5>TRBV20-1	TRGJ2>TRGV8	no clonal rr
14	1	TRAJ40>TRAV17	TRAJ48>TRAV8-3	TRBJ2-1>TRBV28	TRBJ1-2>TRBD1	TRGJ2>TRGV4	TRGJ2>TRGV2
14	2	TRAJ40>TRAV17	TRAJ48>TRAV8-3	TRBJ2-1>TRBV28	TRBJ1-2>TRBD1	TRGJ2>TRGV4	TRGJ2>TRGV2
14	3	TRAJ40>TRAV17	TRAJ48>TRAV8-3	TRBJ2-1>TRBV28	TRBJ1-2>TRBD1	TRGJ2>TRGV4	TRGJ2>TRGV2
15	1	TRAJ53>TRAV27	TRAJ30>TRAV13-2	TRBJ1-5>TRBV5-6	TRBJ1-5>TRBD1	TRGJ2>TRGV4	TRGJ2>TRGV3
15	2	TRAJ53>TRAV27	TRAJ30>TRAV13-2	TRBJ1-5>TRBV5-6	TRBJ1-5>TRBD1	TRGJ2>TRGV4	TRGJ2>TRGV3
16	1	TRAJ20>TRAV34	TRAJ52>TRAV17	TRBJ1-4>TRBD1	TRBJ2-2>TRBD2	TRGJ2>TRGV4	TRGJ2>TRGV2
16	2	TRAJ20>TRAV34	TRAJ52>TRAV17	TRBJ1-4>TRBD1	TRBJ2-2>TRBD2	TRGJ2>TRGV4	TRGJ2>TRGV2
17	1	TRAJ18>TRAV8-3	TRAJ22>TRAV1-1	TRBJ2-1>TRBV3-1	no clonal rr	TRGJP1>TRGV2	TRGJ2>TRGV2
17	2	TRAJ18>TRAV8-3	TRAJ22>TRAV1-1	TRBJ2-1>TRBV3-1	no clonal rr	TRGJP1>TRGV2	TRGJ2>TRGV2
18	1	TRAJ34>TRAV41	TRAJ58>TRAV19	TRBJ2-5>TRBD1	TRBJ2-3>TRBV5-1	TRGJ2>TRGV2	TRGJ2>TRGV3
18	2	TRAJ34>TRAV41	TRAJ58>TRAV19	TRBJ2-5>TRBD1	TRBJ2-3>TRBV5-1	TRGJ2>TRGV2	TRGJ2>TRGV3
19	1	TRAJ12>TRAV9-2	TRAJ27>TRAV38-1	TRBJ2-7>TRBV5-1	TRBJ2-5>TRBV20-1	TRGJ2>TRGV3	TRGJP2>TRGV2
19	2	TRAJ12>TRAV9-2	TRAJ27>TRAV38-1	TRBJ2-7>TRBV5-1	TRBJ2-5>TRBV20-1	TRGJ2>TRGV3	TRGJP2>TRGV2
20	1	TRAJ9>TRAV8-3	TRAJ31>TRAV1-1	TRBJ1-5>TRBV30	TRBJ1-5>TRBD1	TRGJ2>TRGV8	TRGJ2>TRGV5
20	2	TRAJ9>TRAV8-3	TRAJ31>TRAV1-1	TRBJ1-5>TRBV30	TRBJ1-5>TRBD1	TRGJ2>TRGV8	TRGJ2>TRGV5
21	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	TRGJ2>TRGV3	no clonal rr
21	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	TRGJ2>TRGV3	no clonal rr

TCRB
-En 2 pacientes aparece una nueva secuencia (9.5%)

-En 1 paciente se pierde (4.7%)

Figure 3

Patient Number	Sampling Order	IGH Rearrangements		IGK Rearrangements		IGL Rearrangements	
1	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
1	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
2	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
2	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
2	3	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
3	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
3	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
4	1	no clonal rr	no clonal rr	IGKJ5>IGKV3-11	IGKJ3>IGKV3-15	no clonal rr	no clonal rr
4	2	no clonal rr	no clonal rr	IGKJ5>IGKV3-11	IGKJ3>IGKV3-15	no clonal rr	no clonal rr
5	1	no clonal rr	no clonal rr	IGKJ3>IGKV2-28	no clonal rr	no clonal rr	no clonal rr
5	2	no clonal rr	no clonal rr	IGKJ3>IGKV2-28	no clonal rr	no clonal rr	no clonal rr
5	3	no clonal rr	no clonal rr	IGKJ3>IGKV2-28	no clonal rr	no clonal rr	no clonal rr
6	1	IGHJ4>IGHV3-9	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
6	2	IGHJ4>IGHV3-9	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
7	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
8	1	IGHJ6>IGHD2-2	IGHJ6>IGHD6-6	IGKJ1>IGKV3-20	no clonal rr	no clonal rr	no clonal rr
8	2	IGHJ6>IGHD2-2	IGHJ6>IGHD6-6	IGKJ1>IGKV3-20	no clonal rr	no clonal rr	no clonal rr
8	3	IGHJ6>IGHD2-2	IGHJ6>IGHD6-6	IGKJ1>IGKV3-20	no clonal rr	no clonal rr	no clonal rr
8	4	IGHJ6>IGHD2-2	IGHJ6>IGHD6-6	IGKJ1>IGKV3-20	no clonal rr	no clonal rr	no clonal rr
9	1	IGHJ2>IGHD1-26	IGHJ4>IGHD7-27	Kde>IGKV2-28	Kde>IGKV2-29	IGLJ2=J3>IGLV3-21	no clonal rr
9	2	IGHJ2>IGHD1-26	IGHJ4>IGHD7-27	Kde>IGKV2-28	Kde>IGKV2-29	IGLJ2=J3>IGLV3-21	no clonal rr
9	3	IGHJ2>IGHD1-26	IGHJ4>IGHD7-27	Kde>IGKV2-28	Kde>IGKV2-29	IGLJ2=J3>IGLV3-21	no clonal rr
10	1	no clonal rr	no clonal rr	IGKJ3>IGKV2-26	no clonal rr	no clonal rr	no clonal rr
10	2	no clonal rr	no clonal rr	IGKJ3>IGKV2-26	no clonal rr	no clonal rr	no clonal rr
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11	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
12	1	IGHJ3>IGHV3-53	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
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13	1	IGHJ6>IGHD3-9	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
13	2	IGHJ6>IGHD3-9	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
14	1	no clonal rr	no clonal rr	IGKJ1>IGKV5-2	no clonal rr	no clonal rr	no clonal rr
14	2	no clonal rr	no clonal rr	IGKJ1>IGKV5-2	no clonal rr	no clonal rr	no clonal rr
14	3	no clonal rr	no clonal rr	IGKJ1>IGKV5-2	no clonal rr	no clonal rr	no clonal rr
15	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
15	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
16	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
16	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
17	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
17	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
18	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
18	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
19	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
19	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
20	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
20	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
21	1	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr
21	2	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr	no clonal rr

Regular Article

LYMPHOID NEOPLASIA

Clonal germinal center B cells function as a niche for T-cell lymphoma

Manabu Fujisawa,[1] Tran B. Nguyen,[1] Yoshiaki Abe,[2] Yasuhito Suehara,[3] Kota Fukumoto,[1,3] Sakurako Suma,[2] Kenichi Makishima,[2] Chihiro Kaneko,[1] Yen T. M. Nguyen,[1] Kensuke Usuki,[4] Kentaro Narita,[5] Kosei Matsue,[5] Naoya Nakamura,[6] Shumpei Ishikawa,[7] Fumihito Miura,[8] Takashi Ito,[8] Ayako Suzuki,[9] Yutaka Suzuki,[9] Seiya Mizuno,[10] Satoru Takahashi,[10] Shigeru Chiba,[1,3,*] and Mamiko Sakata-Yanagimoto[1,3,11,*]

[1]Department of Hematology, Faculty of Medicine, [2]Department of Hematology, Graduate School of Comprehensive Human Sciences, and [3]Department of Hematology, University of Tsukuba Hospital, University of Tsukuba, Tsukuba, Japan; [4]Department of Hematology, NTT Medical Center Tokyo, Tokyo, Japan; [5]Division of Hematology/Oncology, Department of Internal Medicine, Kameda Medical Center, Kamogawa, Japan; [6]Department of Pathology, Tokai University School of Medicine, Isehara, Japan; [7]Department of Preventive Medicine, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; [8]Department of Biochemistry, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan; [9]Department of Computational Biology and Medical Sciences, Graduate School of Frontier Sciences, The University of Tokyo, Kashiwa, Japan; and [10]Laboratory Animal Resource Center and [11]Division of Advanced Hemato-Oncology, Transborder Medical Research Center, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

KEY POINTS

- **ACH-derived GCB cells with aberrant expression profiles underwent independent clonal evolution in the microenvironment of AITL.**
- **Inhibition of the CD40–CD40LG axis, as revealed by in silico network analysis, is a potential novel therapeutic target.**

Angioimmunoblastic T-cell lymphoma (AITL) is proposed to be initiated by age-related clonal hematopoiesis (ACH) with *TET2* mutations, whereas the G17V *RHOA* mutation in immature cells with *TET2* mutations promotes the development of T follicular helper (T_{FH})-like tumor cells. Here, we investigated the mechanism by which *TET2*-mutant immune cells enable AITL development using mouse models and human samples. Among the 2 mouse models, mice lacking *Tet2* in all the blood cells (*Mx-Cre* × *Tet2*$^{flox/flox}$ × G17V *RHOA* transgenic mice) spontaneously developed AITL for approximately up to a year, while mice lacking *Tet2* only in the T cells (*Cd4-Cre* × *Tet2*$^{flox/flox}$ × G17V *RHOA* transgenic mice) did not. Therefore, *Tet2*-deficient immune cells function as a niche for AITL development. Single-cell RNA-sequencing (scRNA-seq) of >50 000 cells from mouse and human AITL samples revealed significant expansion of aberrant B cells, exhibiting properties of activating light zone (LZ)-like and proliferative dark zone (DZ)-like germinal center B (GCB) cells. The GCB cells in AITL clonally evolved with recurrent mutations in genes related to core histones. In silico network analysis using scRNA-seq data identified Cd40–Cd40lg as a possible mediator of GCB and tumor cell cluster interactions. Treatment of AITL model mice with anti-Cd40lg inhibitory antibody prolonged survival. The genes expressed in aberrantly expanded GCB cells in murine tumors were also broadly expressed in the B-lineage cells of *TET2*-mutant human AITL. Therefore, ACH-derived GCB cells could undergo independent clonal evolution and support the tumorigenesis in AITL via the CD40–CD40LG axis.

Introduction

The discovery of age-related clonal hematopoiesis (ACH) has resulted in a paradigm shift in research on hematopoiesis in aging. ACH occurs when hematopoietic stem/progenitor cells (HSPCs) acquire somatic mutations, particularly in genes encoding epigenetic regulators, such as *DNMT3A*, *TET2*, and *ASXL1*.[1] They frequently occur in various age-related diseases such as diabetes, ischemic heart disease, atherosclerosis, as well as hematological and solid cancers.[2] Various lineages of immune cells with somatic mutations derived from ACH infiltrate cancer tissues[3,4]; however, their function in cancer development remains poorly understood.

Angioimmunoblastic T-cell lymphoma (AITL), a neoplasm of mature T cells,[5] is a representative cancer derived from ACH. Genetically, loss-of-function *TET2* mutations occur in HSPCs,[6] which then acquire disease-specific p.Gly17Val *RHOA* mutations leading to T-lineage tumor development.[7,8] Pathologically, as the name "immunoblast" implies, AITL tissues are characterized by abundant infiltration of B immunoblasts.[9] AITL tumor cells exhibit characteristics of T follicular helper (T_{FH}) cells,[10] which are physiologically localized in lymph node (LN) follicles and mainly interact with germinal center B (GCB) cells to facilitate their maturation and function.[11-14]

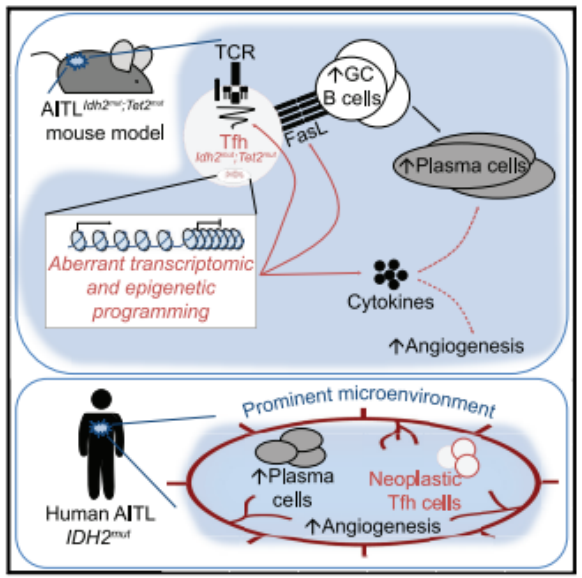
Here, we investigated how ACH-derived immune cells are involved in AITL pathogenesis by using originally established mouse models and human samples. Single-cell RNA-sequencing analysis (scRNA-seq) revealed the marked expansion of

Cancer Cell

Article

IDH2 and TET2 mutations synergize to modulate T Follicular Helper cell functional interaction with the AITL microenvironment

Graphical abstract



Authors

Julie Leca, François Lemonnier, Cem Meydan, ..., Ari Melnick, Philippe Gaulard, Tak W. Mak

Correspondence

julie.leca@uhnresearch.ca (J.L.), tak.mak@uhnresearch.ca (T.W.M.)

In brief

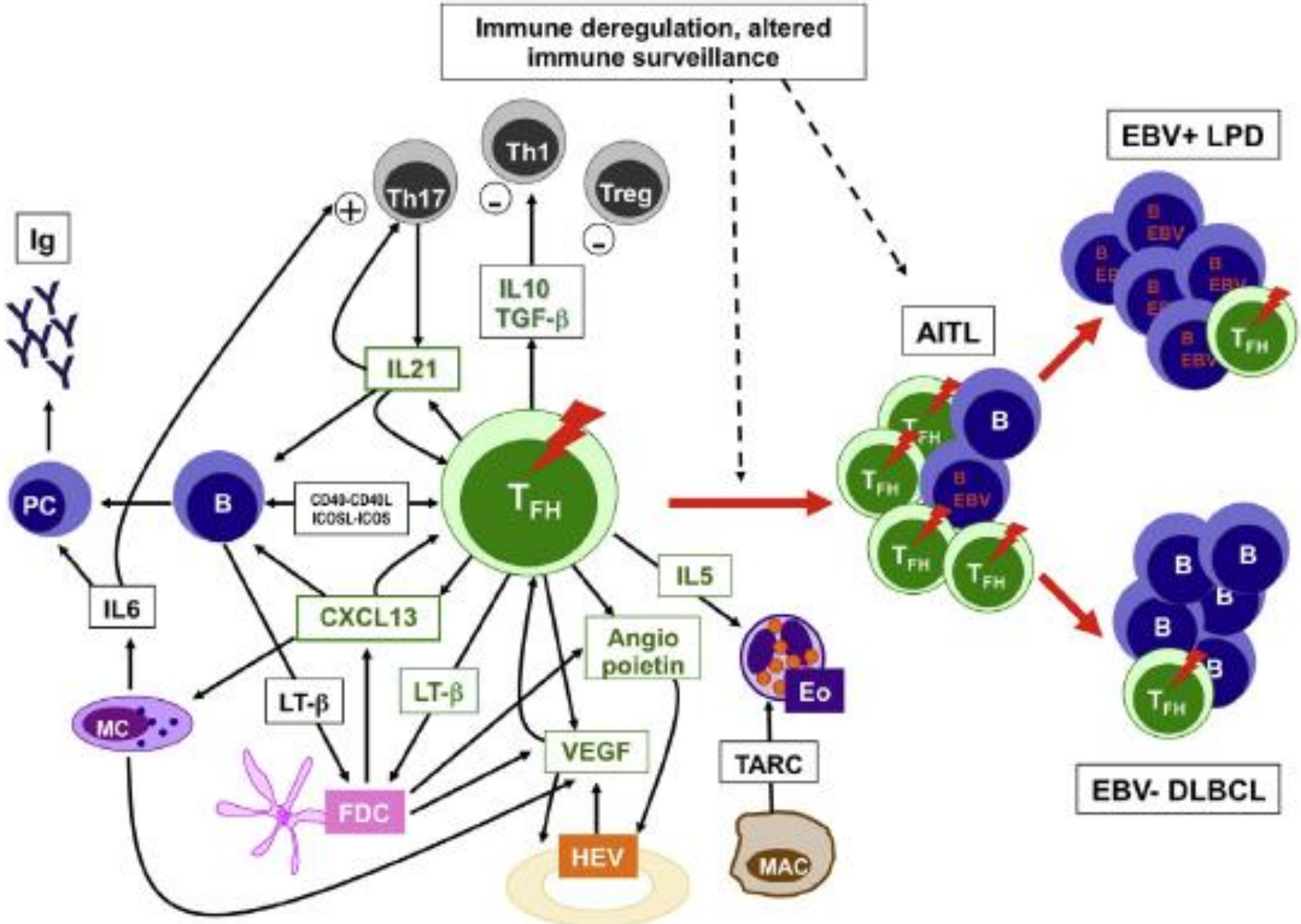
Leca et al. show that combining *Idh2* and *Tet2* mutations in mouse T cells leads to an AITL-like disease that recapitulates features of human AITL. These two mutations synergize at the transcriptomic and epigenetic levels to alter the functions of Tfh cells and their relationship with the tumor microenvironment.

Highlights

- ***Idh2*;*Tet2*-mutated T cells induce AITL after transplantation into recipient mice**
- ***Idh2*;*Tet2* mutations alter Tfh cell transcriptomics and epigenetics**
- ***Idh2*;*Tet2* mutations alter Tfh cell phenotype/function, normal B cells, and the TME**
- **Combined *Idh2*;*Tet2* mutation downregulates FasL signaling in Tfh cells**

Leca et al., 2023, Cancer Cell *41*, 323–339
February 13, 2023
https://doi.org/10.1016/j.ccell.2023.01.003

CellPress


Immune deregulation, altered immune surveillance
Th1
Th17
Treg
Ig
IL10
TGF-β
IL21
PC
B
CD40-CD40L
ICOSL-ICOS
TFH
IL6
CXCL13
IL5
Angio poietin
LT-β
LT-β
MC
FDC
VEGF
HEV
Eo
TARC
MAC
AITL
EBV+ LPD
EBV- DLBCL

ESTUDIOS FUTURO

-Transcriptómica y secuenciacion sobre grupos de células según localización espacial en tejido (material parafinado).

-Transcriptómica y secuenciación en célula única (sorter…). Material en fresco.

-Modelos tridimensionales, esferoides….

-Validación clínica (serie de pacientes)

Secuenciación masiva de genoma completo. Grupo del Dr E Campo. Hospital Clinic. Barcelona. "MEDICINA DE PRECISIÓN GENÓMICA EN NEOPLASIAS LINFOIDES (PREGENLIF)"

bjh research paper

Clinical and pathological characteristics of peripheral T-cell lymphomas in a Spanish population: a retrospective study

Socorro Maria Rodriguez-Pinilla,[1] Eva Domingo-Domenech,[2] Fina Climent,[3] Joaquin Sanchez,[4] Carlos Perez Seoane,[4] Javier Lopez Jimenez,[5] Monica Garcia-Cosio,[6] Dolores Caballero,[7] Oscar Javier Blanco Muñez,[8] Cecilia Carpio,[9] Josep Castellvi,[10] Antonio Martinez Pozo,[11] Blanca Gonzalez Farre,[12] Angeles Bendaña,[13] Carlos Aliste,[13] Ana Julia Gonzalez,[14] Sonia Gonzalez de Villambrosia,[15] Miguel A. Piris,[16] Jose Gomez Codina,[17] Empar Mayordomo-Aranda,[17] Belen Navarro,[18] Carmen Bellas,[19] Guillermo Rodriguez,[20] Juan Jose Borrero,[20] Ana Ruiz-Zorrilla,[21] Marta Grande,[21] Carmen Montoto[21] and Raul Cordoba[22]

[1]*Pathology Department, Hospital Universitario Fundación Jiménez Díaz, Madrid,CIBERONC, Madrid,* [2]*Hematology Department, Institut Català d'Oncologia L'Hospitalet de Llobregat (Barcelona),* [3]*Pathology Department, Hospital Universitari de Bellvitge. IDIBELL, L'Hospitalet de Llobregat (Barcelona), Barcelona,* [4]*Hematology Department and Pathology Department, Hospital Universitario Reina Sofía, Cordoba,* [5]*Hematology Department, Hospital Universitario Ramón y Cajal, Madrid,* [6]*Anatomical Pathology Department, Hospital Universitario Ramón y Cajal, Madrid,CIBERONC, Madrid,* [7]*Hematology Department, Hospitalario Universitario de Salamanca (HUS/IBSAL) and CIBERONC, Salamanca,* [8]*Pathology Department, Complejo Asistencial Universitario de Salamanca-IBSAL, Salamanca,* [9]*Hematology Department, Hospital Universitari Vall d'Hebron,* [10]*Pathology Department, Hospital*

Abstract

We investigated the clinicopathological features and prognostic factors of patients with peripheral T-cell lymphoma (PTCL) in 13 sites across Spain. Relevant clinical antecedents, CD30 expression and staining pattern, prognostic indices using the International Prognostic Index and the Intergruppo Italiano Linfomi system, treatments, and clinical outcomes were examined. A sizeable proportion of 175 patients had a history of immune-related disorders (autoimmune 16%, viral infections 17%, chemo/radiotherapy-treated carcinomas 19%). The median progression-free survival (PFS) and overall survival (OS) were 7·9 and 15·8 months, respectively. Prognostic indices influenced PFS and OS, with a higher number of adverse factors resulting in shorter survival ($P < 0·001$). Complete response (CR) to treatment was associated with better PFS (62·6 vs. 4 months; $P < 0·001$) and longer OS (67·0 vs. 7·3 months; $P < 0·001$) compared to no CR. CD30 was expressed across all subtypes; >15% of cells were positive in anaplastic lymphoma kinase-positive and -negative anaplastic large-cell lymphoma and extranodal natural killer PTCL groups. We observed PTCL distribution across subtypes based on haematopathological re-evaluation. Poor prognosis, effect of specific prognostic indices, relevance of histopathological subclassification, and response level to first-line treatment on outcomes were confirmed. Immune disorders amongst patients require further examination involving genetic studies and identification of associated immunosuppressive factors.

Keywords: peripheral T-cell lymphoma, anaplastic lymphoma kinase, anaplastic large-cell lymphoma, progression-free survival, overall survival, complete response.

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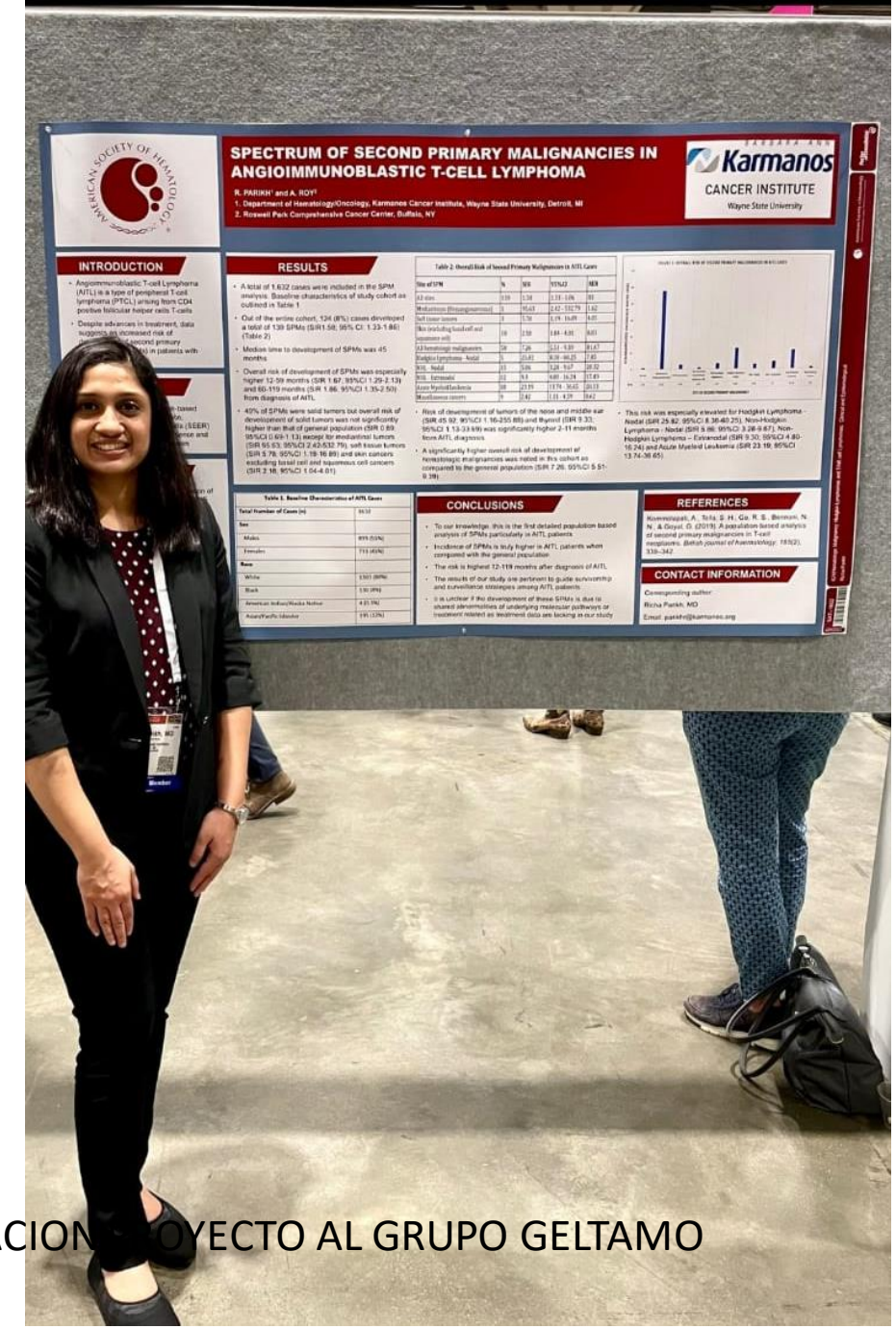

PRESENTACION PROYECTO AL GRUPO GELTAMO

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DOI: 10.1111/cas.15165

ORIGINAL ARTICLE

Cancer Science WILEY

Tet2 deficiency in immune cells exacerbates tumor progression by increasing angiogenesis in a lung cancer model

Yen T. M. Nguyen[1] | Manabu Fujisawa[2] | Tran B. Nguyen[2] | Yasuhito Suehara[3] | Tatsuhiro Sakamoto[2,3] | Ryota Matsuoka[4] | Yoshiaki Abe[1] | Kota Fukumoto[3] | Keiichiro Hattori[3] | Masayuki Noguchi[4] | Daisuke Matsubara[4,5] | Shigeru Chiba[2,3] | Mamiko Sakata-Yanagimoto[2,3]

[1]Department of Hematology, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tsukuba, Japan

[2]Department of Hematology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

[3]Department of Hematology, University of Tsukuba Hospital, Tsukuba, Japan

[4]Department of Pathology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

[5]Department of Pathology, Jichi Medical University, Shimotsuke, Japan

Correspondence
Mamiko Sakata-Yanagimoto, Department of Hematology, Faculty of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8575, Japan.
Email: sakatama@md.tsukuba.ac.jp

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Abstract

Immune cells harboring somatic mutations reportedly infiltrate cancer tissues in patients with solid cancers and accompanying clonal hematopoiesis. Loss-of-function *TET2* mutations are frequently observed in clonal hematopoiesis in solid cancers. Here, using a mouse lung cancer model, we evaluated the activity of *Tet2*-deficient immune cells in tumor tissues. Myeloid-specific *Tet2* deficiency enhanced tumor growth in mice relative to that seen in controls. Single-cell sequencing analysis of immune cells infiltrating tumors showed relatively high expression of S100a8/S100a9 in *Tet2*-deficient myeloid subclusters. In turn, treatment with S100a8/S100a9 promoted Vegfa production by cancer cells, leading to a marked increase in the tumor vasculature in *Tet2*-deficient mice relative to controls. Finally, treatment of *Tet2*-deficient mice with an antibody against Emmprin, a known S100a8/S100a9 receptor, suppressed tumor growth. These data suggest that immune cells derived from *TET2*-mutated clonal hematopoiesis exacerbate lung cancer progression by promoting tumor angiogenesis and may provide a novel therapeutic target for lung cancer patients with *TET2*-mutated clonal hematopoiesis.

KEYWORDS

angiogenesis, Emmprin, immune cells, lung cancer, S100a8, S100a9, *Tet2*, Vegfa

PRESENTACION PROYECTO AL GRUPO GELTAMO
Dr Manel Esteller. Josep Carreras Leukaemia Research Institute, Barcelona.

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The DNA methylcytosine dioxygenase Tet2 sustains the immunosuppressive function of tumor-infiltrating myeloid cells to promote melanoma progression

Wen Pan[1,2], **Shu Zhu**[3,4], **Kun Qu**[4], **Katrina Meeth**[5,6], **Jijun Cheng**[1,2], **Kaixin He**[4], **Hongdi Ma**[4], **Yan Liao**[7], **Xizhi Wen**[8], **Christine Roden**[1,2], **Zuzana Tobiasova**[3], **Zheng Wei**[3], **Jun Zhao**[3], **Jun Liu**[1,2], **Ji Zheng**[1,2], **Bo Guo**[1,9], **Sajid A. Khan**[10], **Marcus Bosenberg**[5,6], **Richard A. Flavell**[3], and **Jun Lu**[1,2,11]

[1]Department of Genetics, Yale University School of Medicine, New Haven, CT 06520, USA

[2]Yale Stem Cell Center, Yale Cancer Center, Yale Cooperative Center of Excellence in Hematology, Yale University, New Haven, CT, 06520, USA

[3]Department of Immunobiology, Yale University School of Medicine, New Haven, CT 06520

[4]Institute of Immunology and the CAS Key Laboratory of Innate Immunity and Chronic Disease, School of Life Sciences and Medical Center, University of Science and Technology of China, Hefei, 230027, China

[5]Department of Pathology, Yale University School of Medicine, New Haven, CT 06519, USA

[6]Department of Dermatology, Yale University School of Medicine, New Haven, CT 06519, USA

[7]Center for Stem Cell Biology and Tissue Engineering, Key Laboratory for Stem Cells and Tissue Engineering, Ministry of Education, Sun Yat-Sen University, Guangzhou, 510060, China

[8]Biotherapy Center, Sun Yat-Sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, Guangzhou, 510060, China

[9]General Hospital of People's Liberation Army, Beijing, China

[10]Department of Surgery, Yale University School of Medicine, New Haven, CT 06519, USA

Summary

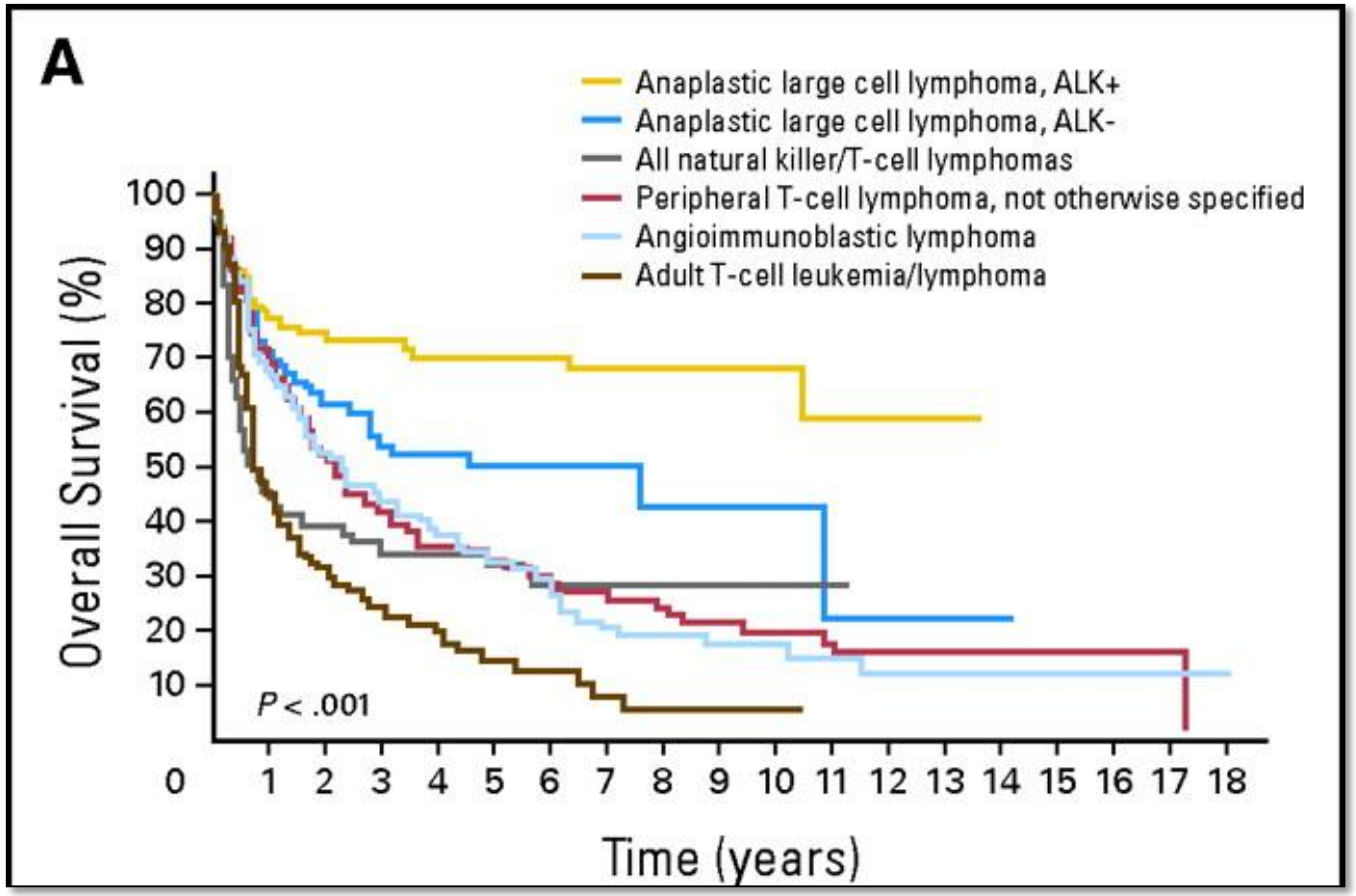
Ten-Eleven-Translocation-2 (Tet2) is a DNA methylcytosine dioxygenase that functions as a tumor suppressor in hematopoietic malignancies. In this study, we revealed a role for Tet2 in sustaining the immunosuppressive function of tumor-tissue myeloid cells. We found that *Tet2* expression is

[11]Lead contact and correspondence: Jun Lu, 10 Amistad Street, Room 237C, New Haven, CT 06520-8005. Telephone: 203-737-3426; Fax: 203-785-4305; jun.lu@yale.edu.

hor Contributions: W.P. designed and conducted most of the experiments. S.Z., K.M. J.C., K.H., H.M., Z.W., C.R. J.Liu, Z.T., and B.G. participated in the experiments. K.Q., J.Z. W.P. and J.Lu performed bioinformatics analysis. Y.L., X.W. collected and yzed human samples. M.B., R.F. and S.K. assisted with reagents, experimental design and data interpretation. J.Lu supervised the y. J.Lu. and W.P. wrote the manuscript.

IMPLICACIÓN PRONÓSTICA

Overall survival of patients with the common subtypes of peripheral T-cell lymphoma (PTCL)



International T-Cell Lymphoma Project, J Clin Oncol; 26:4124-4130 2008

bjh research paper

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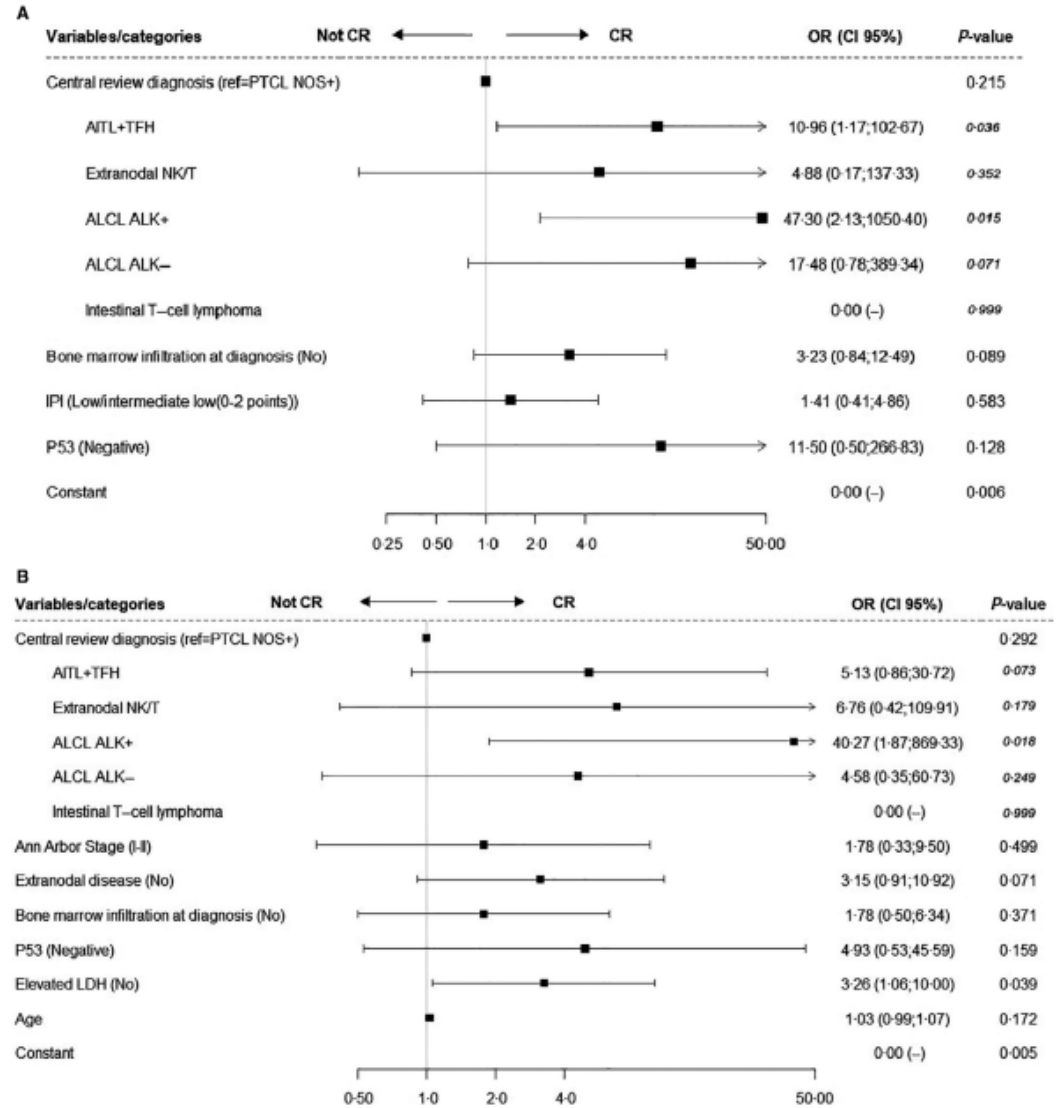
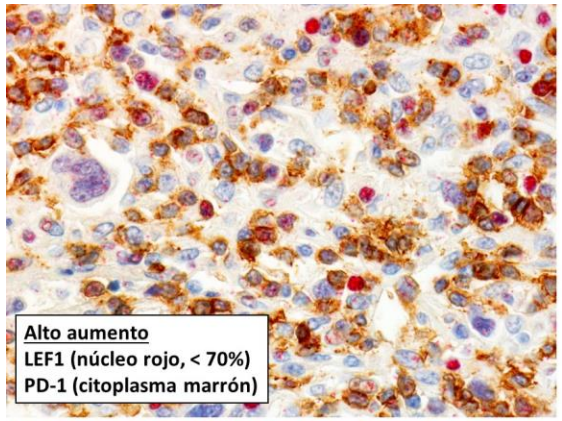
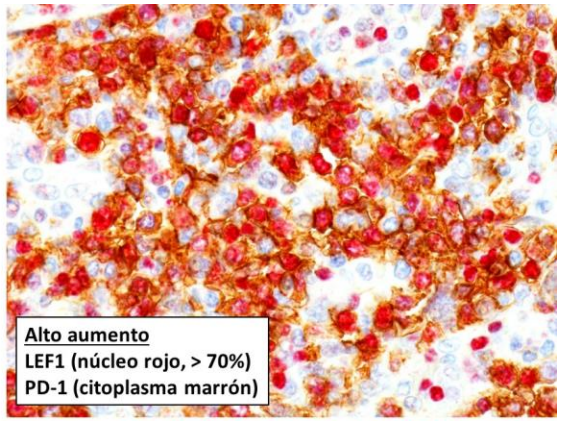
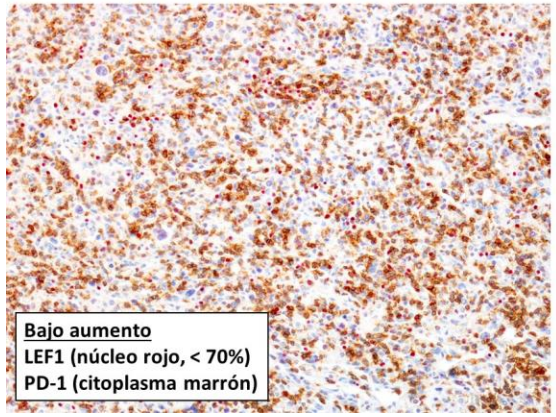


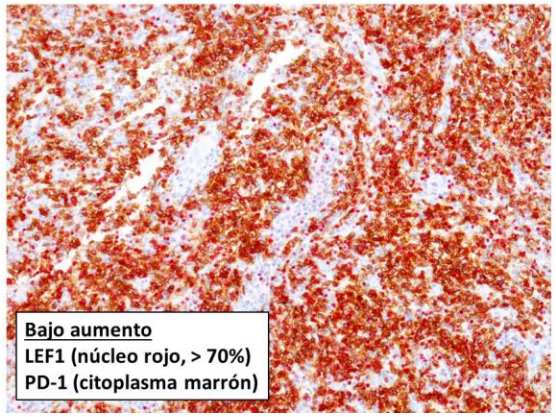
Fig 5. Multivariate logistic regression model for complete response (CR) to first-line treatment. (A) Multivariate logistic regression model on the probability of reaching CR to first-line treatment considering all factors with $P < 0·1$ in the univariate analysis, and excluding factors already included in the IPI calculation. (B) Probability of reaching a CR factors used in the IPI calculation (excluding IPI). **Reference factor. OR, odds ratio; CI, confidence interval; AITL, angioimmunoblastic T-cell Lymphoma; ALK+ ALCL, anaplastic lymphoma kinase (ALK)-positive anaplastic large-cell lymphoma; ALK– ALCL, ALK-negative ALCL; PTCL, peripheral TCL; NOS, not otherwise specified; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IPI, International prognostic index; PIT, Prognostic Index for T-Cell Lymphoma.

La expresión de LEF1 por encima del 70 % parece correlacionarse con una mayor tasa de recaídas o progresión al tratamiento









	LEF1 < 70 % (n = 33)	LEF1 ≥ 70 % (n = 39)	*p*
Primera línea de tratamiento	N (%)	N (%)	
Respuesta completa	15 (48,4)	16 (51,6)	0,146*
Respuesta parcial	8 (44,4)	10 (55,6)	
Estabilidad de la enfermedad	2 (33,3)	4 (66,7)	
Progresión de la enfermedad	3 (25,0)	9 (75,0)	
Recaída o progresión al tratamiento	12 (33,3)	24 (66,7)	0,045*
Segunda línea de tratamiento	N (%)	N (%)	
Respuesta completa	3 (50,0)	3 (50,0)	0,286*
Respuesta parcial	4 (30,8)	9 (69,2)	
Estabilidad de la enfermedad	1 (25,0)	3 (75,0)	
Progresión de la enfermedad	5 (33,3)	10 (66,7)	
Recaída o progresión al tratamiento	6 (33,3)	12 (66,7)	0,040*

EXPRESIÓN GÉNICA

Respondedores vs No respondedores

ESQUEMA

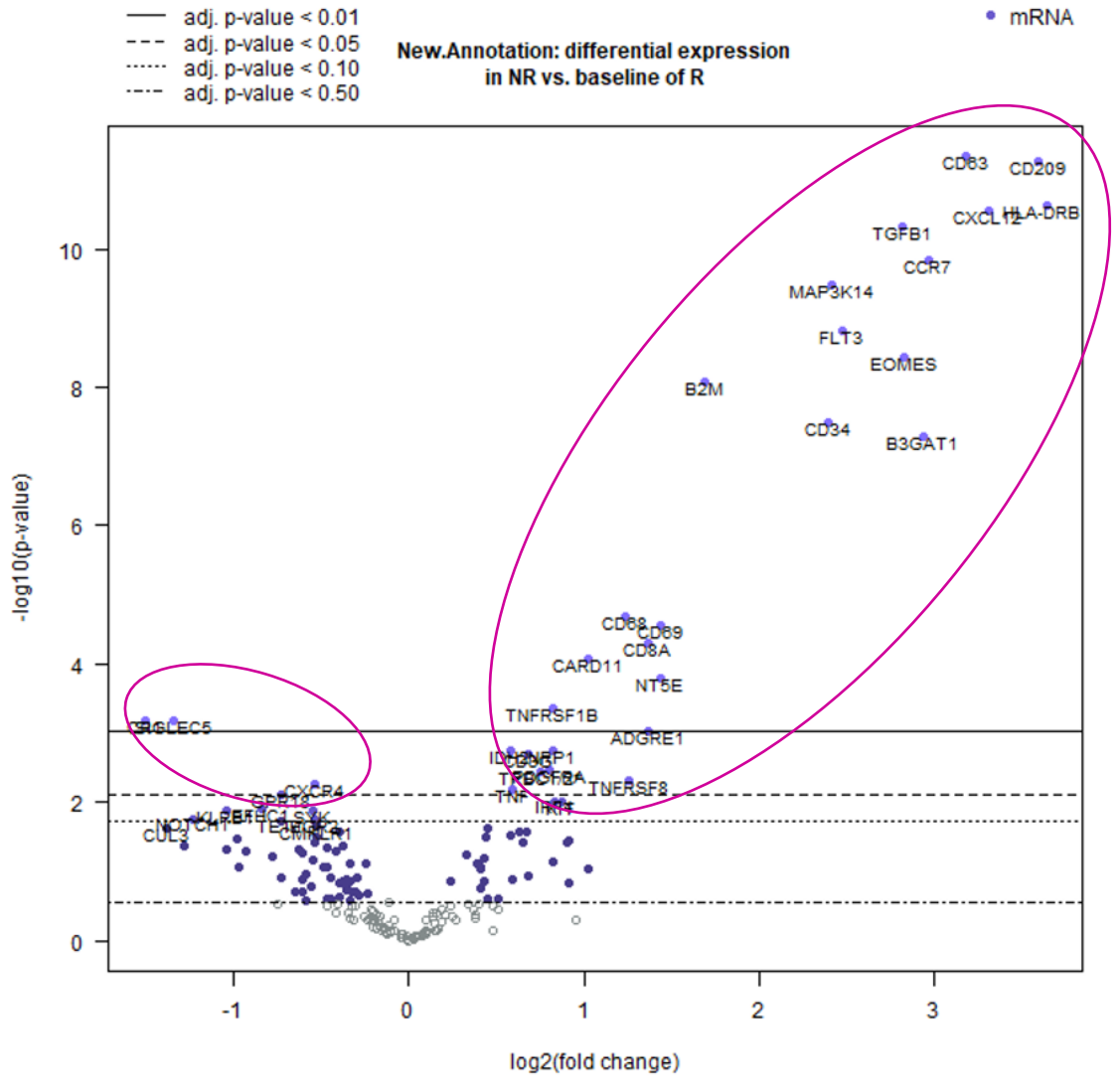
SERIE ESTUDIO

SERIE VALIDACIÓN

Completa (PTCL-NOS,PTCL-THF, AITL)	PTCL- THF y AITL	Completa (PTCL-NOS,PTCL-THF, AITL)	PTCL- THF y AITL
1	2	3	4

1. SERIE ESTUDIO COMPLETA

Volcano Plot



Respondedores

SIGLEC5
CR1
CXCR4
GPR18

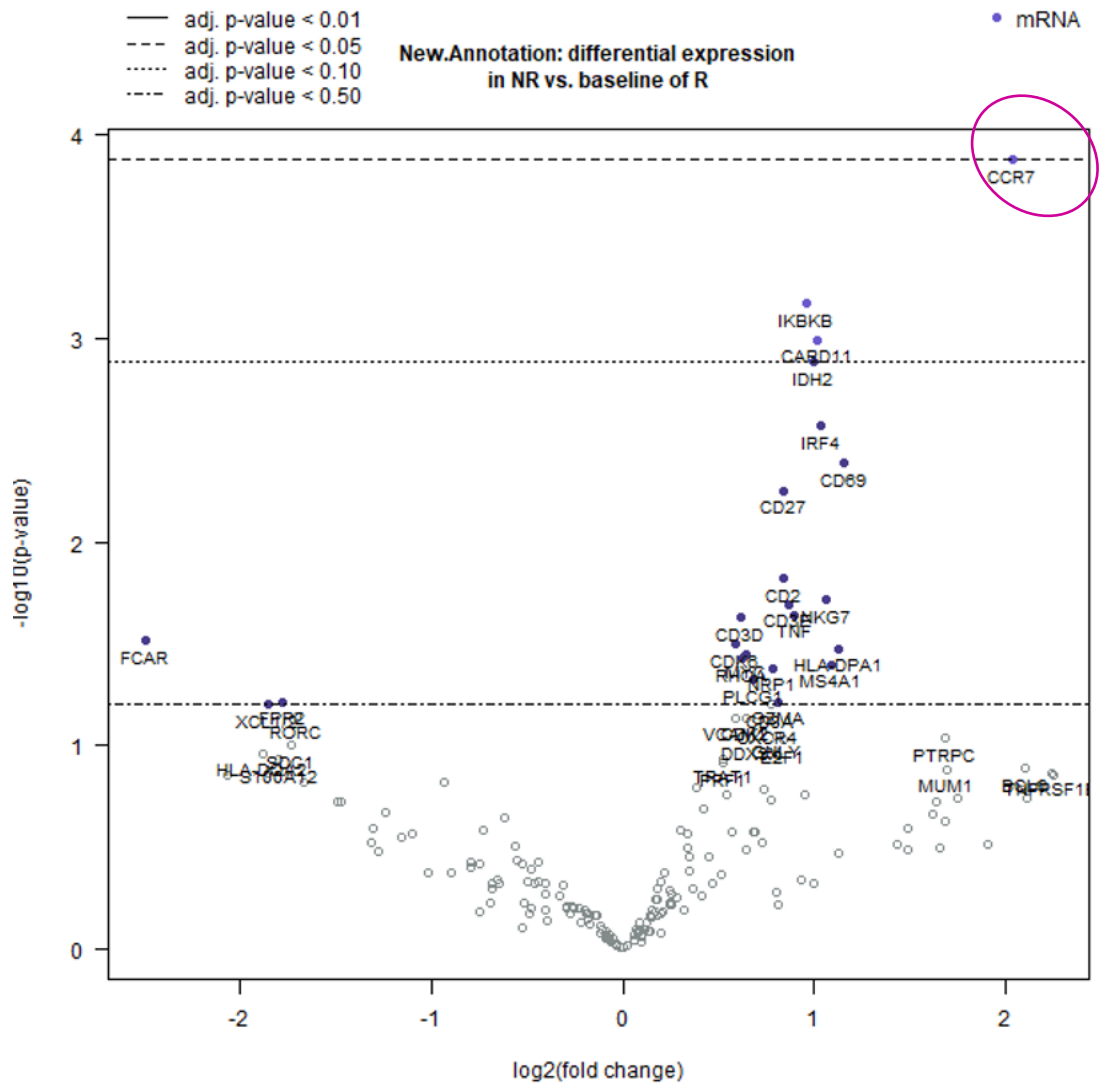
No Respondedores

CD63
CD209
HLA-DRB1
CXCL12
TGFB1
CCR7
MAP3K14
FLT3
EOMES
B2M
CD34
B3GAT1
CD68
CD69
CD8A
CARD11
NT5E
TNFRSF1B

3.SERIE VALIDACIÓN COMPLETA

Volcano Plot

Respondedores



No Respondedores

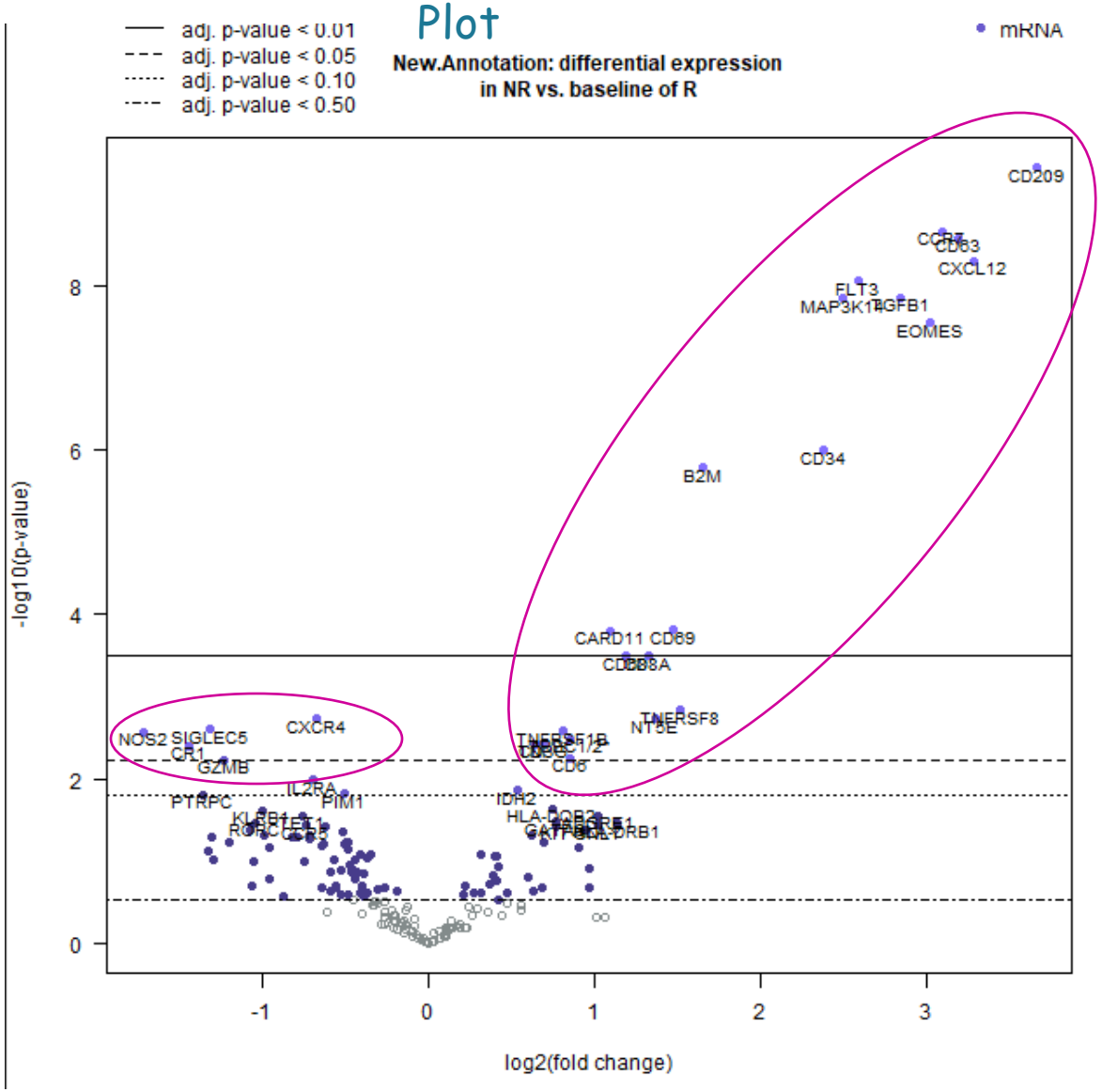
CCR7

2. SERIE ESTUDIO (AITL y PTCL-TFH)

Respondedores

CXCR4
SIGLEC5
NOS2
CR1
GZMB

Volcano Plot



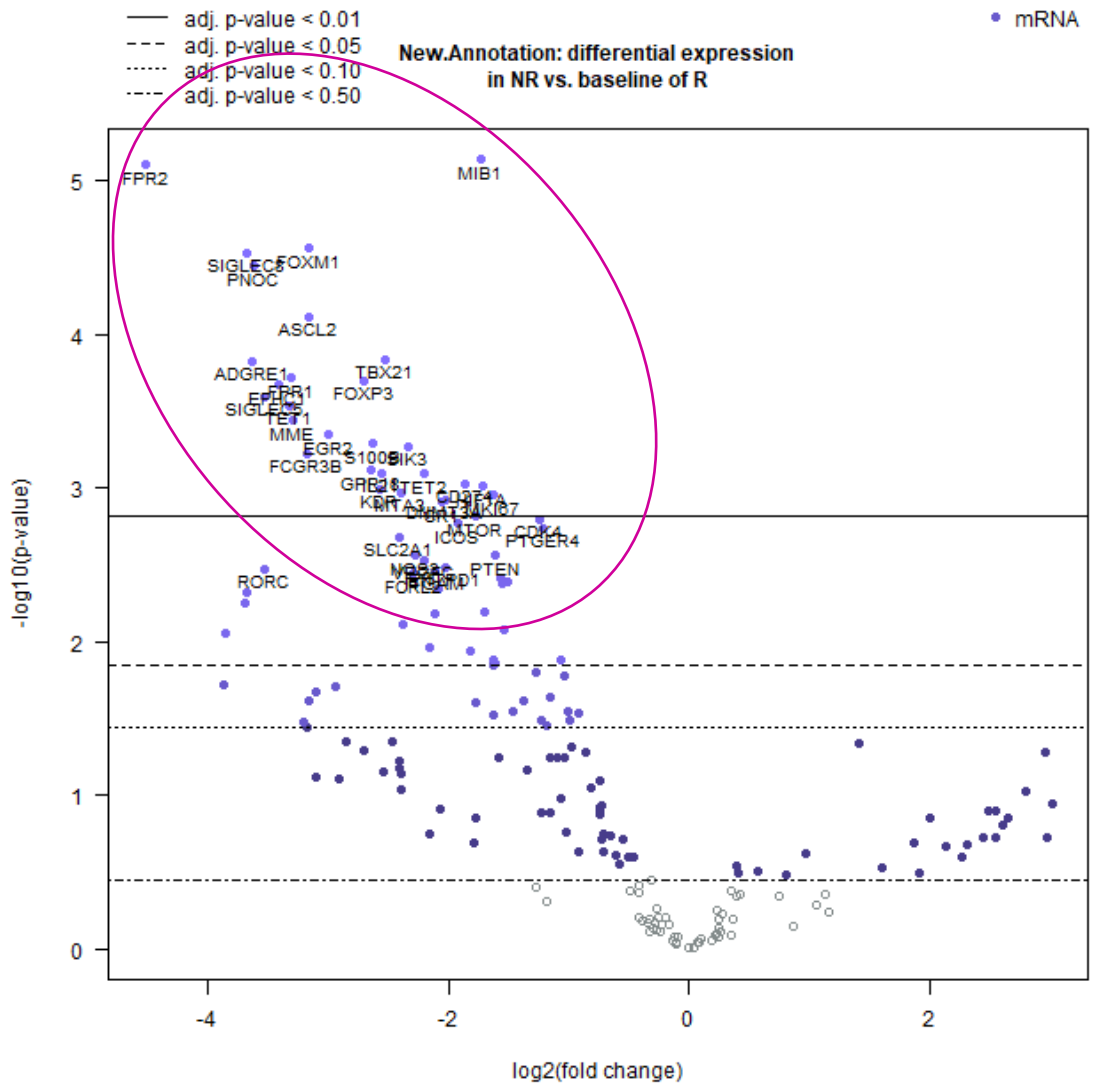
No Respondedores

CD209
CCR7
CD63
CXCL12
FLT3
TGFB1
MAP3K14
EOMES
CD34
B2M
CD69
CARD11
CD68
CD8A
TNFRSF8

4. SERIE VALIDACIÓN (AITL y PTCL-TFH)

Respondedores

MIB1
FPR2
FOXM
SIGLEC8
PNOC
ASCL2
TBX21
ADGRE1
FPR1
FOXP3
EFHC1
SIGLEC5
TET1
MME
EGR2
S100B
SIK3
FCGR3B
GPR18
IL21



No Respondedores

MUTACIONES

Respondedores vs No respondedores

PERFIL MUTACIONAL

Gene	p value
RESPONSE * TNFRSF1B	0.0029
RESPONSE * KRAS	0.0304
RESPONSE * PRKCQ	0.0304
RESPONSE * IDH2	0.0665
RESPONSE * IRF4	0.1008
RESPONSE * VAV1	0.1498
RESPONSE * EZH2	0.2094
RESPONSE * MTOR	0.2316
RESPONSE * JAK2	0.2546
RESPONSE * JAK3	0.2546
RESPONSE * RARA	0.2546
RESPONSE * CXCL12	0.2578
RESPONSE * RHOA	0.3060
RESPONSE * TP53	0.3160
RESPONSE * SMARCA4	0.3895
RESPONSE * PRKCB	0.3895
RESPONSE * CD28	0.4863
RESPONSE * FOXM1	0.4863
RESPONSE * BCOR	0.5145
RESPONSE * TSC1	0.5145
RESPONSE * CD58	0.6255
RESPONSE * PLCG1	0.6255
RESPONSE * SIK3	0.6255
RESPONSE * EPHB6	0.6255
RESPONSE * MAPK1	0.6255
RESPONSE * NRAS	0.6255
RESPONSE * CD274	0.6255
RESPONSE * EFHC1	0.6255
RESPONSE * CDKN2A	0.6255
RESPONSE * STAT5B	0.6255
RESPONSE * SYK	0.6255
RESPONSE * ZEB1	0.7363
RESPONSE * NOTCH1	0.7363
RESPONSE * STAT3	0.7497
RESPONSE * DNMT3A	0.7645
RESPONSE * JAK1	0.8794
RESPONSE * ATM	0.8794
RESPONSE * TET2	0.8841
RESPONSE * ARID1B	0.9269
RESPONSE * ARID1A	0.9508
RESPONSE * CARD11	0.9508
RESPONSE * DDX3X	0.9508
RESPONSE * PTPRN2	0.9508
RESPONSE * NCOR1	0.9508

Genes mutados asociados a No respuesta

Serie completa

AITL+PTCL-TFH

Gene	p value
RESPONSE * EZH2	0.00100
RESPONSE * KRAS	0.01500
RESPONSE * IRF4	0.01500
RESPONSE * PRKCQ	0.01500
RESPONSE * TNFRSF1B	0.02200
RESPONSE * IDH2	0.04100
RESPONSE * JAK2	0.18800
RESPONSE * JAK3	0.18800
RESPONSE * RARA	0.18800
RESPONSE * BCOR	0.18800
RESPONSE * ZEB1	0.24800
RESPONSE * MTOR	0.34376
RESPONSE * VAV1	0.34400
RESPONSE * ARID1A	0.41100
RESPONSE * TSC1	0.41100
RESPONSE * CXCL12	0.43000
RESPONSE * PRKCB	0.43000
RESPONSE * RHOA	0.45200
RESPONSE * CD28	0.52400
RESPONSE * SMARCA4	0.52400
RESPONSE * CARD11	0.62400
RESPONSE * PTPRN2	0.62400
RESPONSE * NCOR1	0.62400
RESPONSE * STAT3	0.62400
RESPONSE * TET2	0.64400
RESPONSE * SIK3	0.65500
RESPONSE * TP53	0.65500
RESPONSE * FOXM1	0.65500
RESPONSE * MAPK1	0.65500
RESPONSE * NRAS	0.65500
RESPONSE * PLCG1	0.65500
RESPONSE * CDKN2A	0.65500
RESPONSE * STAT5B	0.65500
RESPONSE * SYK	0.65500
RESPONSE * EPHB6	0.65538
RESPONSE * DDX3X	0.81500
RESPONSE * ATM	0.81500
RESPONSE * DNMT3A	0.85500
RESPONSE * ARID1B	0.87500
RESPONSE * JAK1	0.98100
RESPONSE * NOTCH1	0.98100

GRACIAS

aecc
Contra el Cáncer

Hospital Universitario
Fundación Jiménez Díaz
Grupo quirónsalud

Itziar Eraña

Salma Machan
Juan Torres
Luis Requena

Comunidad de Madrid