Monthly Multi-Institutional Hematopathology Interesting Case Conference

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FOX CHASE CANCER CENTER
TEMPLE HEALTH

Case Presentation

78-year-old Caucasian male with h/o chronic thrombocytopenia, prostate cancer s/p prostatectomy, melanoma in situ,

Presenting Complaint (August 2025)

- **Diffuse lymphadenopathy** (bilateral axillary, cervical, inguinal; largest 3.6 cm) without B symptoms.

- **Pancytopenia** (WBC 1.4 x 10^9/L, Hb 11.6 g/dL, platelets 32 x 10^9/L)

Imaging

Multi-station diffuse lymphadenopathy

Bilateral Cervical and axillary Lymphadenopathy

- R axillary: **3.6 × 1.6 cm**

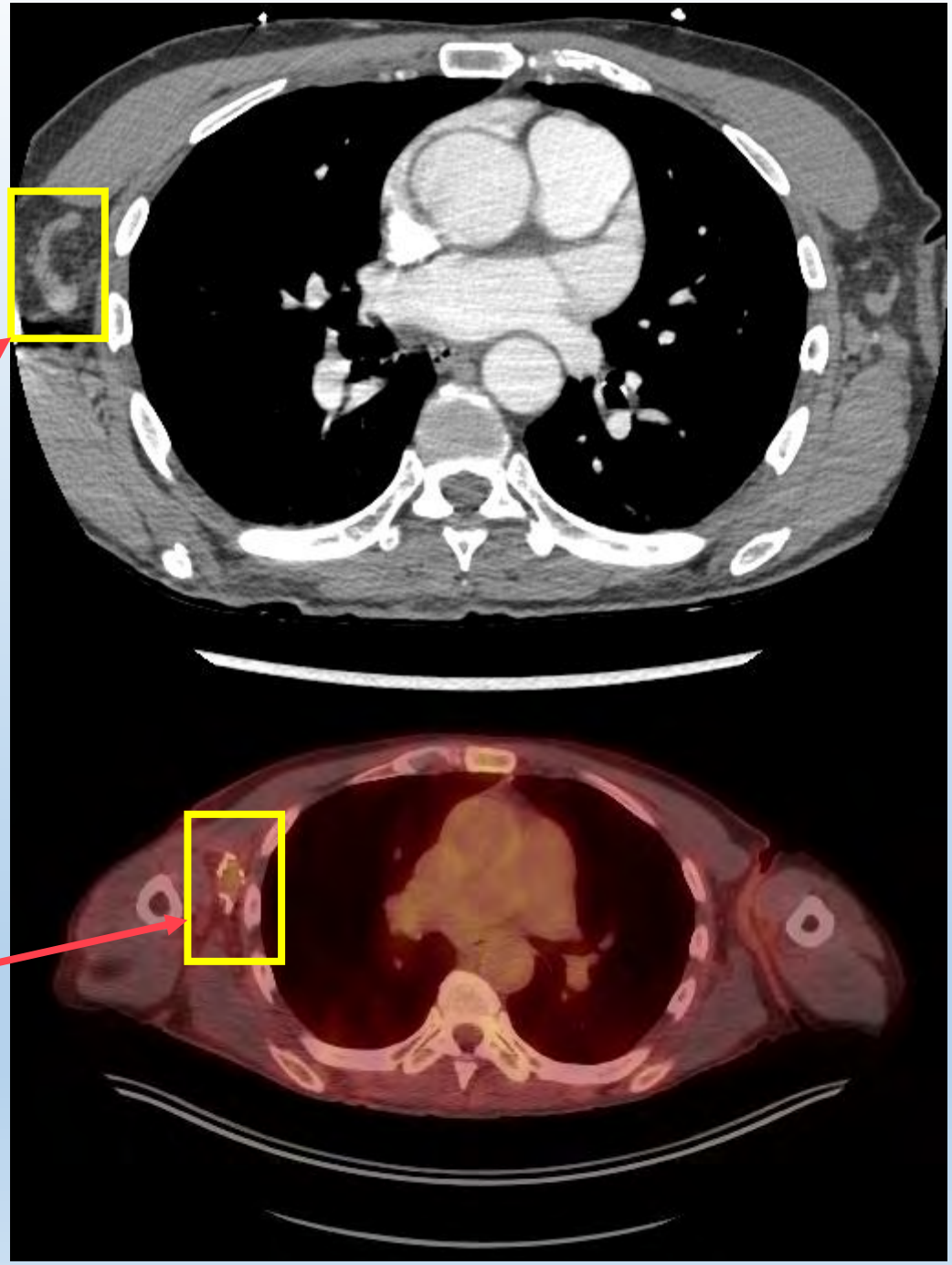
Retroperitoneal, mesenteric, pelvic, L inguinal nodes

• Hepatomegaly: 20.7 cm

• Splenomegaly: 17.2 cm

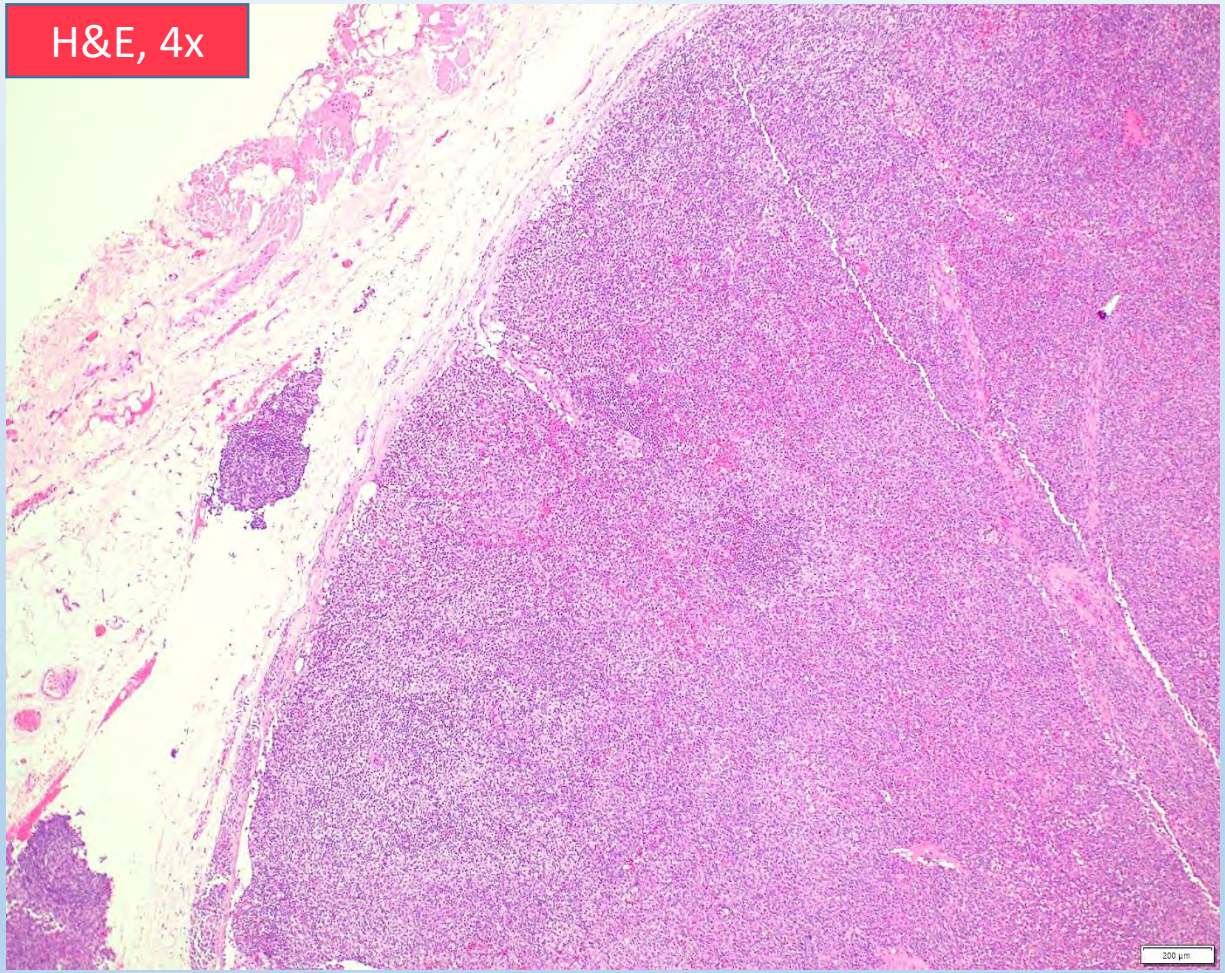
PET-CT:

• Mild-moderate FDG avidity **(SUV max 5.2),** no bulky disease

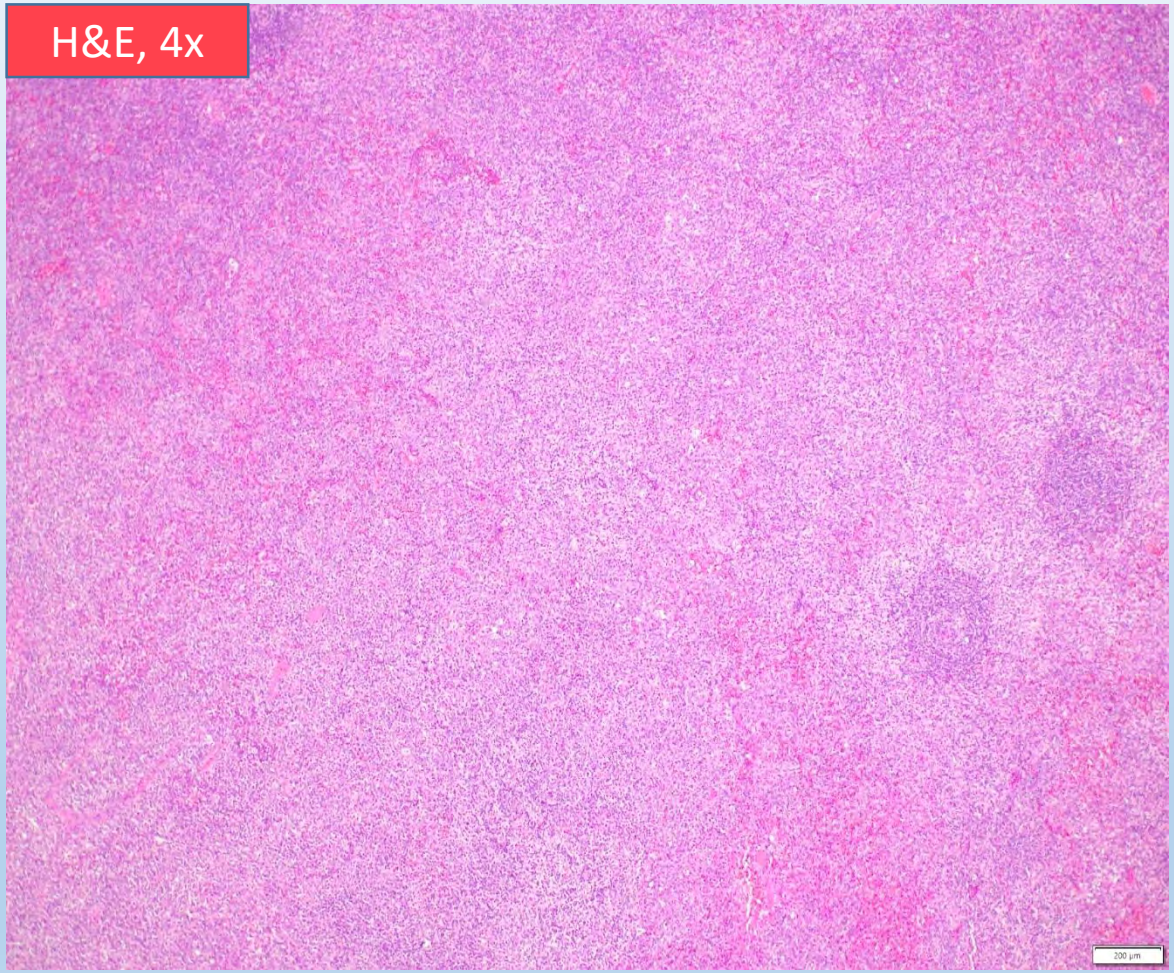


Excisional: Right axillary Lymph node (Sept 2025)

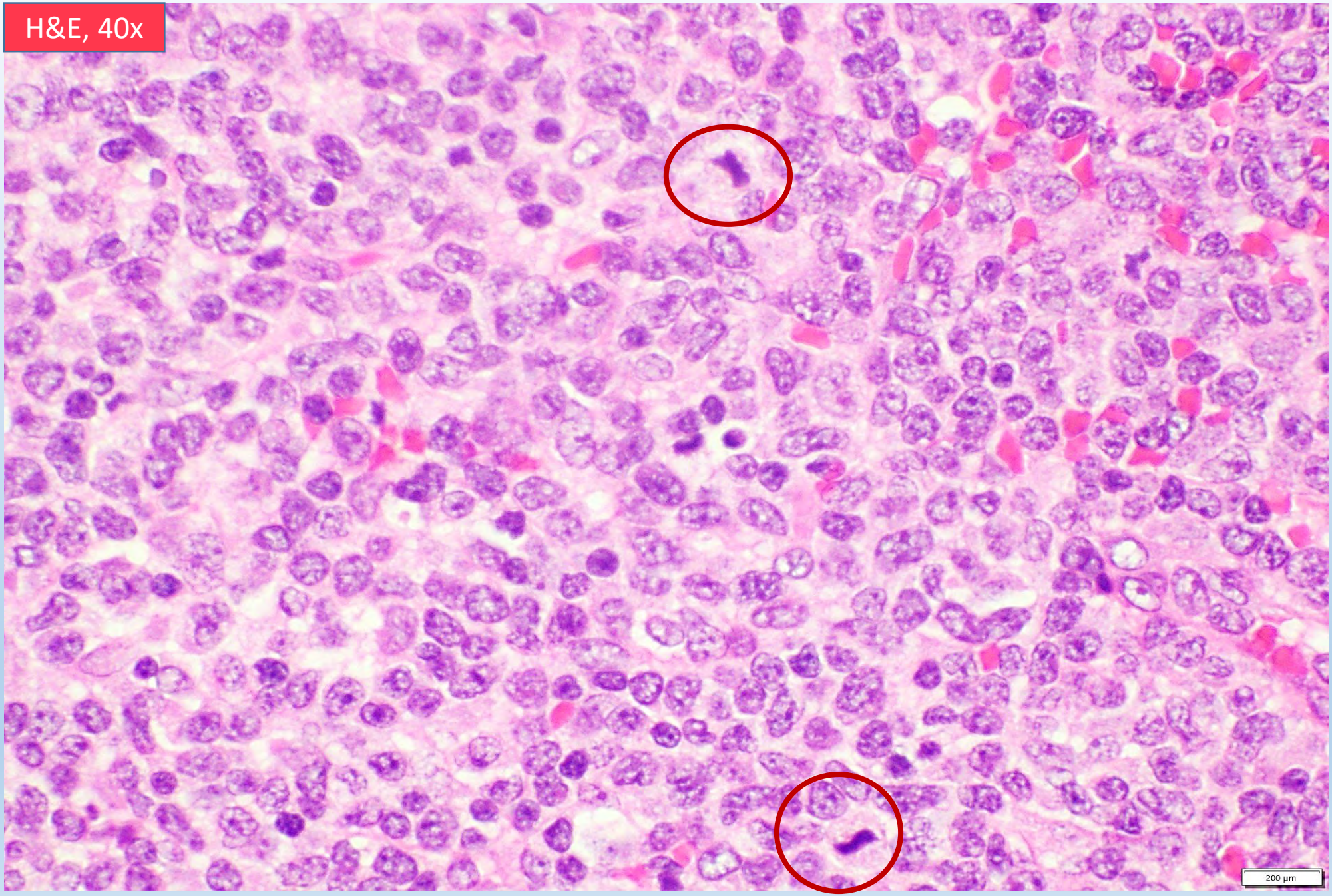
H&E, 4x



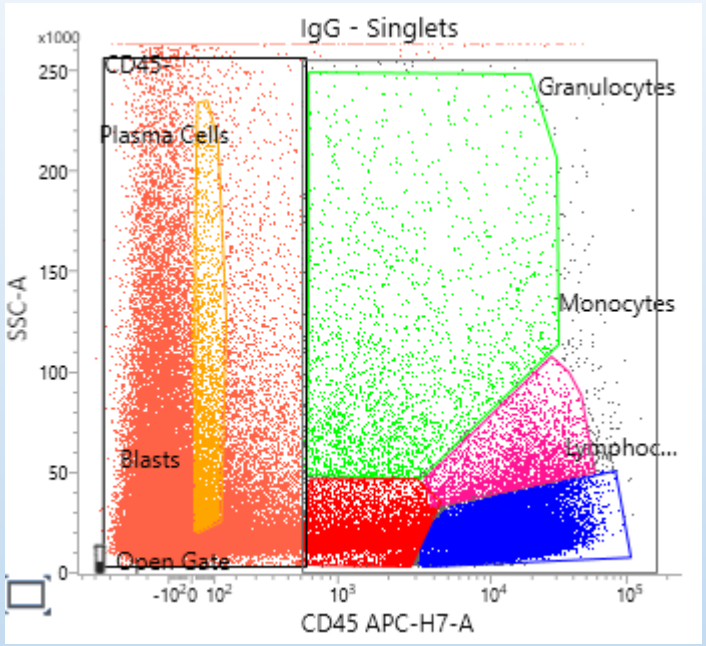
H&E, 4x



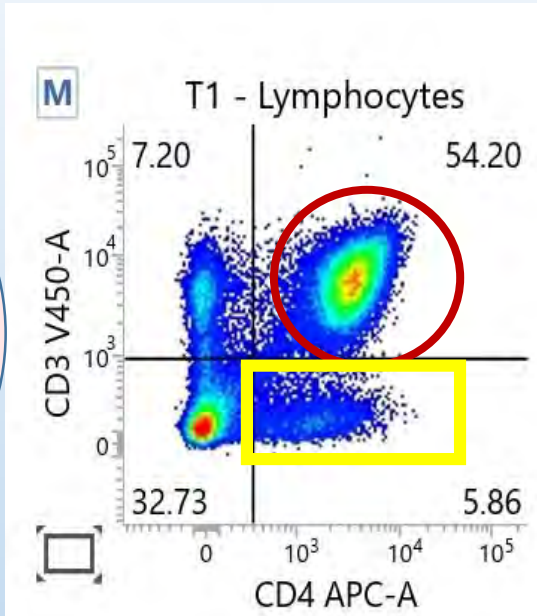
Partial effacement of the architecture by paracortical and interfollicular expansion

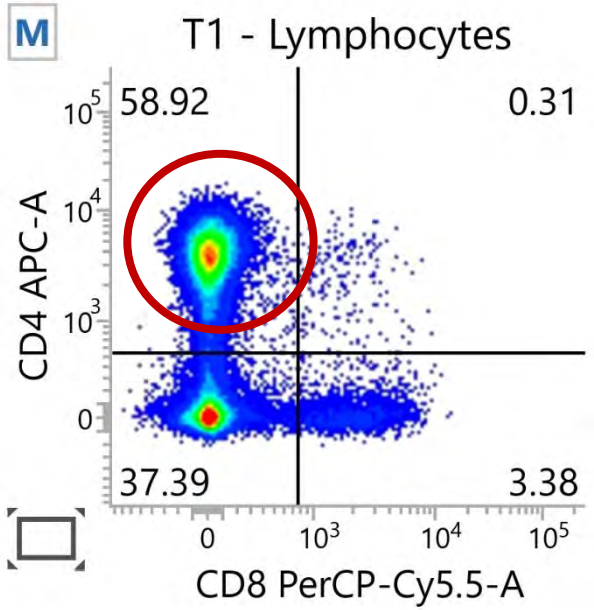

H&E, 40x
200 µm

Flow cytometry: Right axillary Lymph node



Elevated CD4:CD8 ratio (15:1)



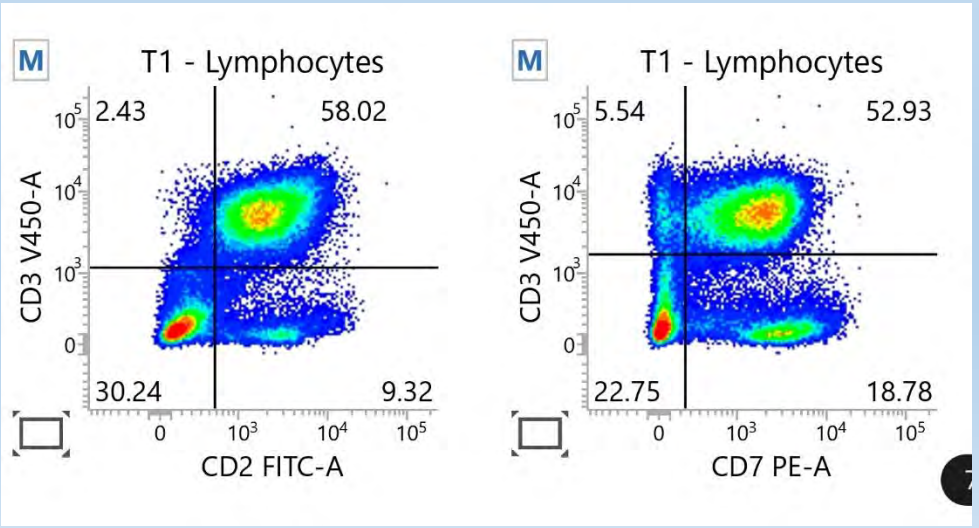


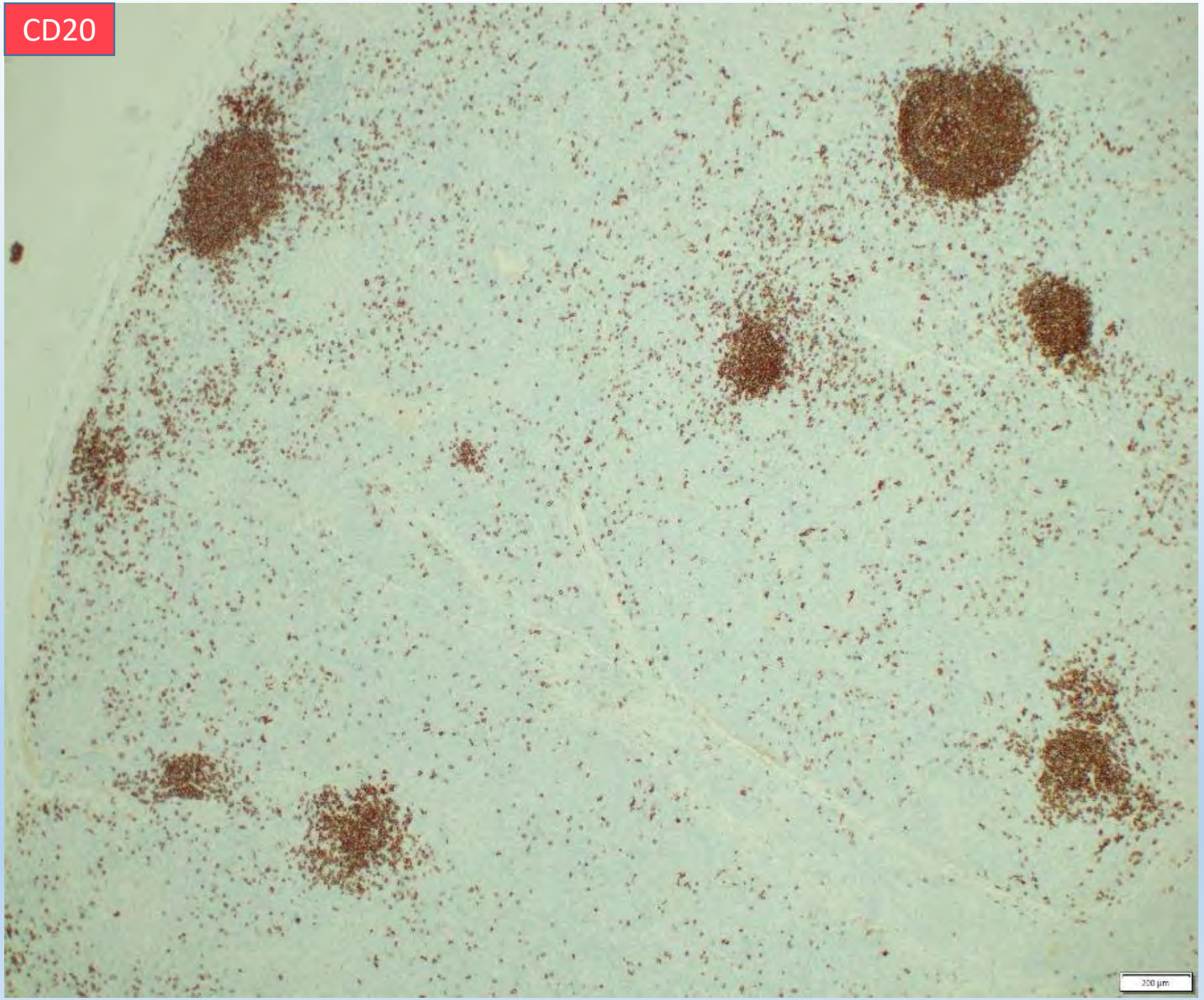
CD4+ population (60% of lymphocytes) with

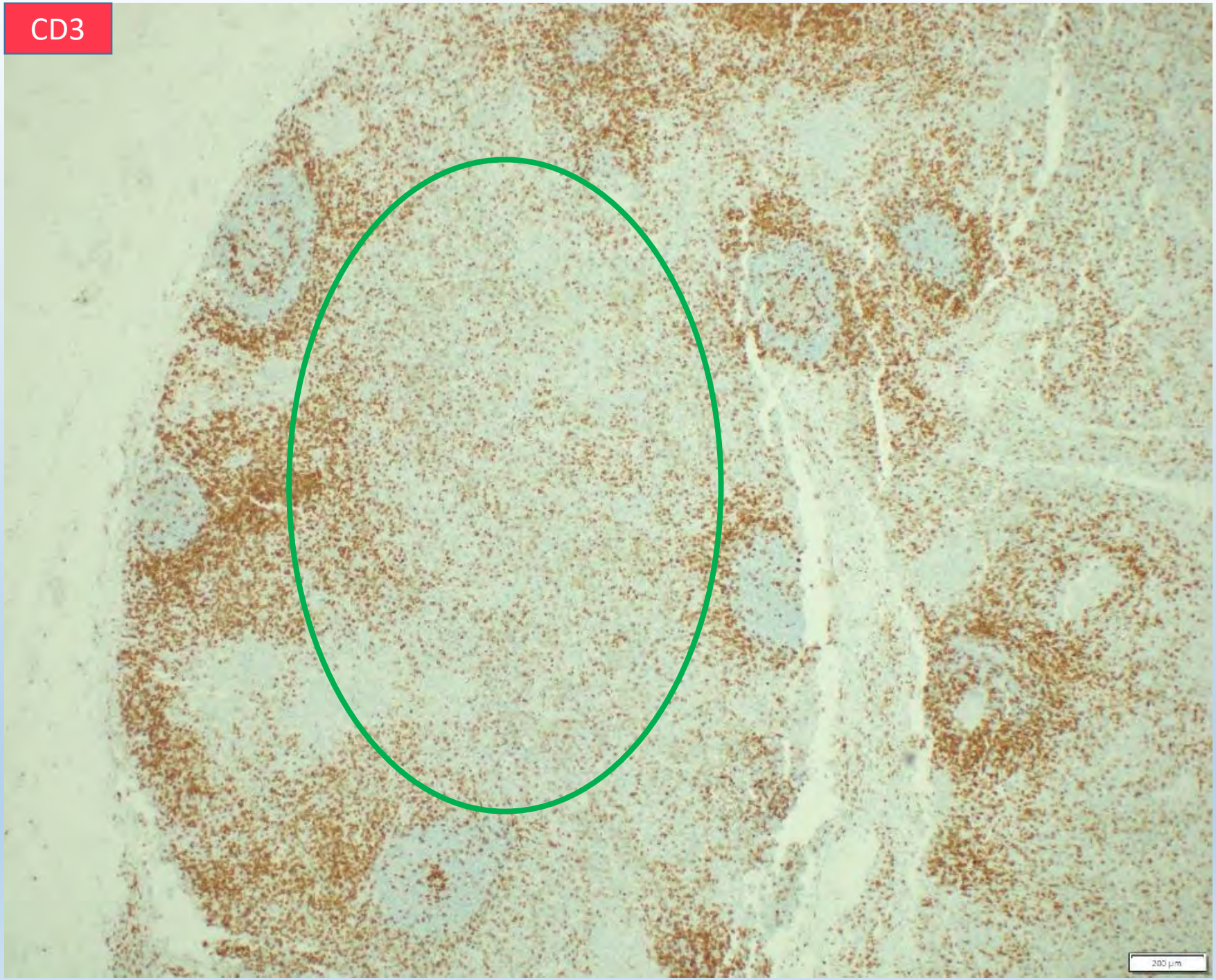
a small subset (6% of lymphocytes) showing aberrant loss of CD3 expression.

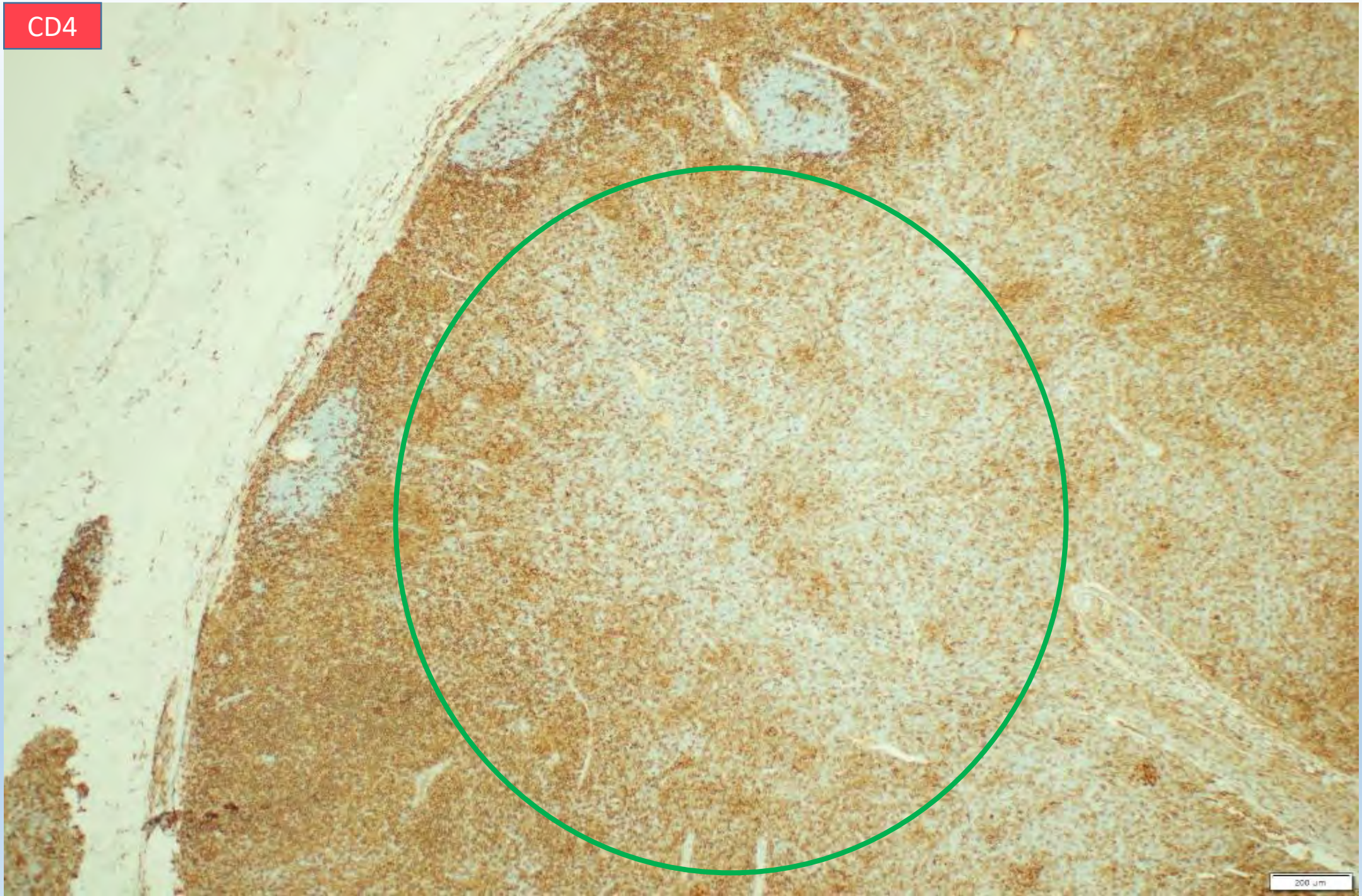
Expanded panel:

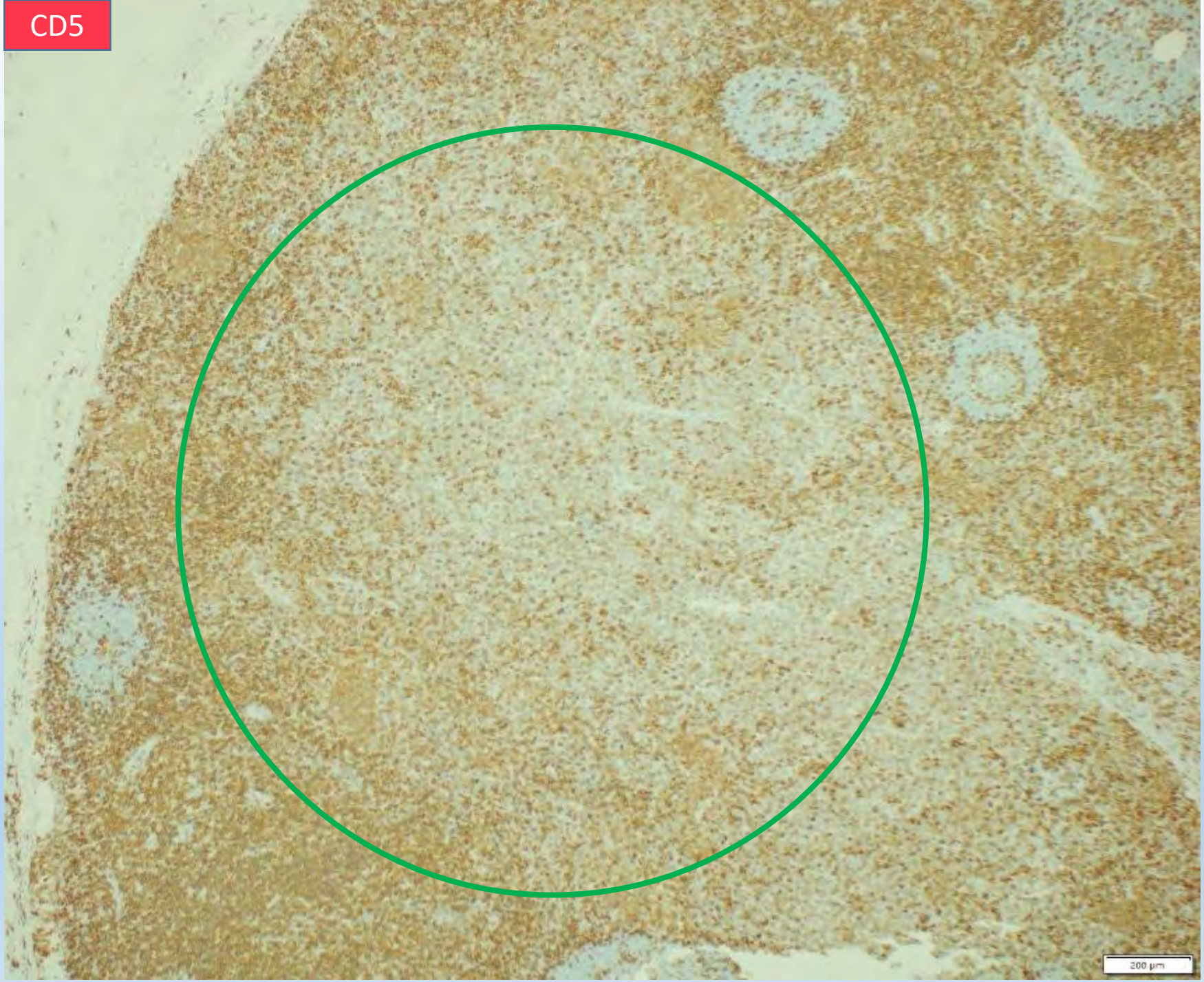
Low events → Suboptimal further characterization of aberrant CD3- CD4+ T-cell subsets

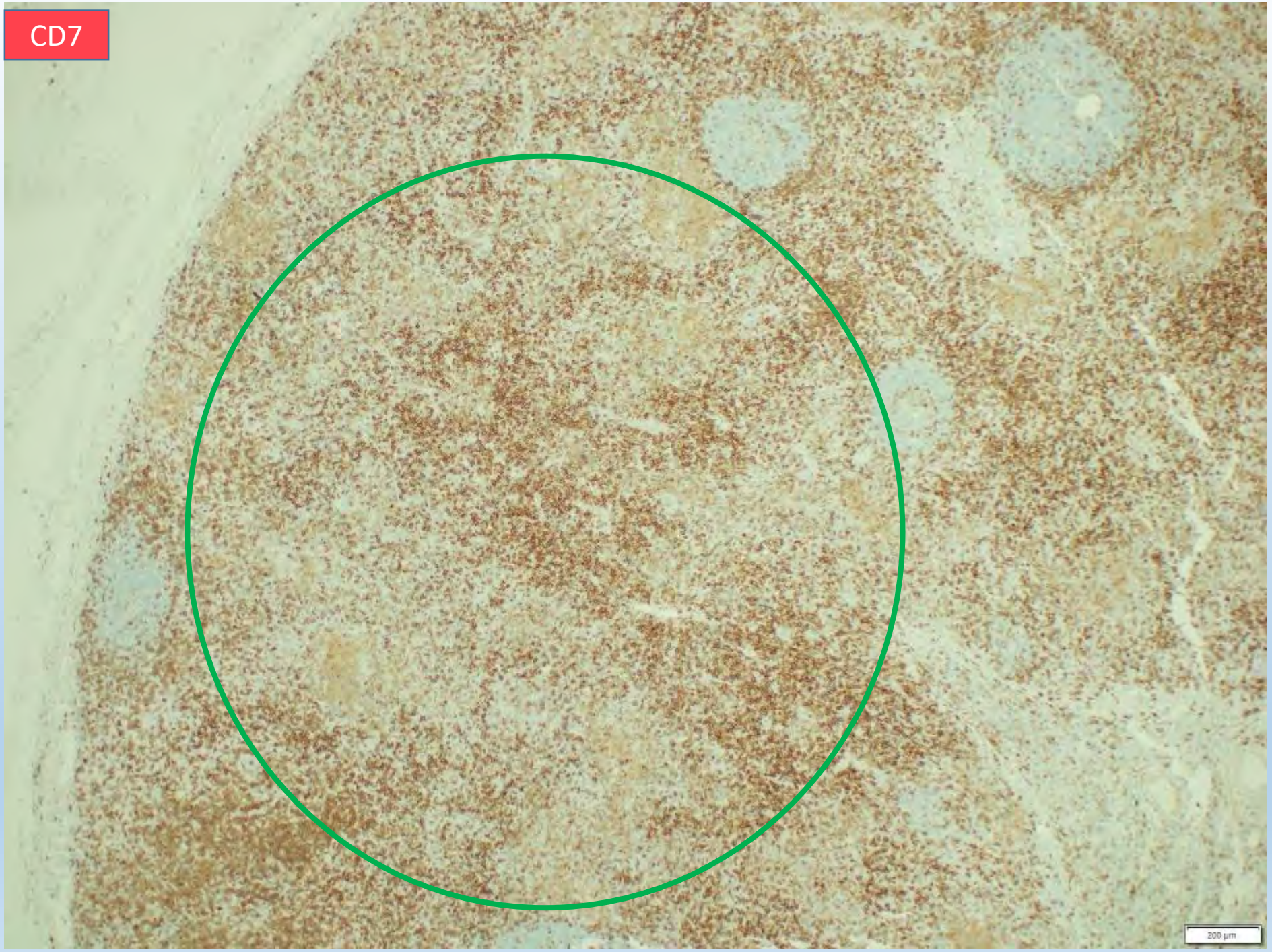


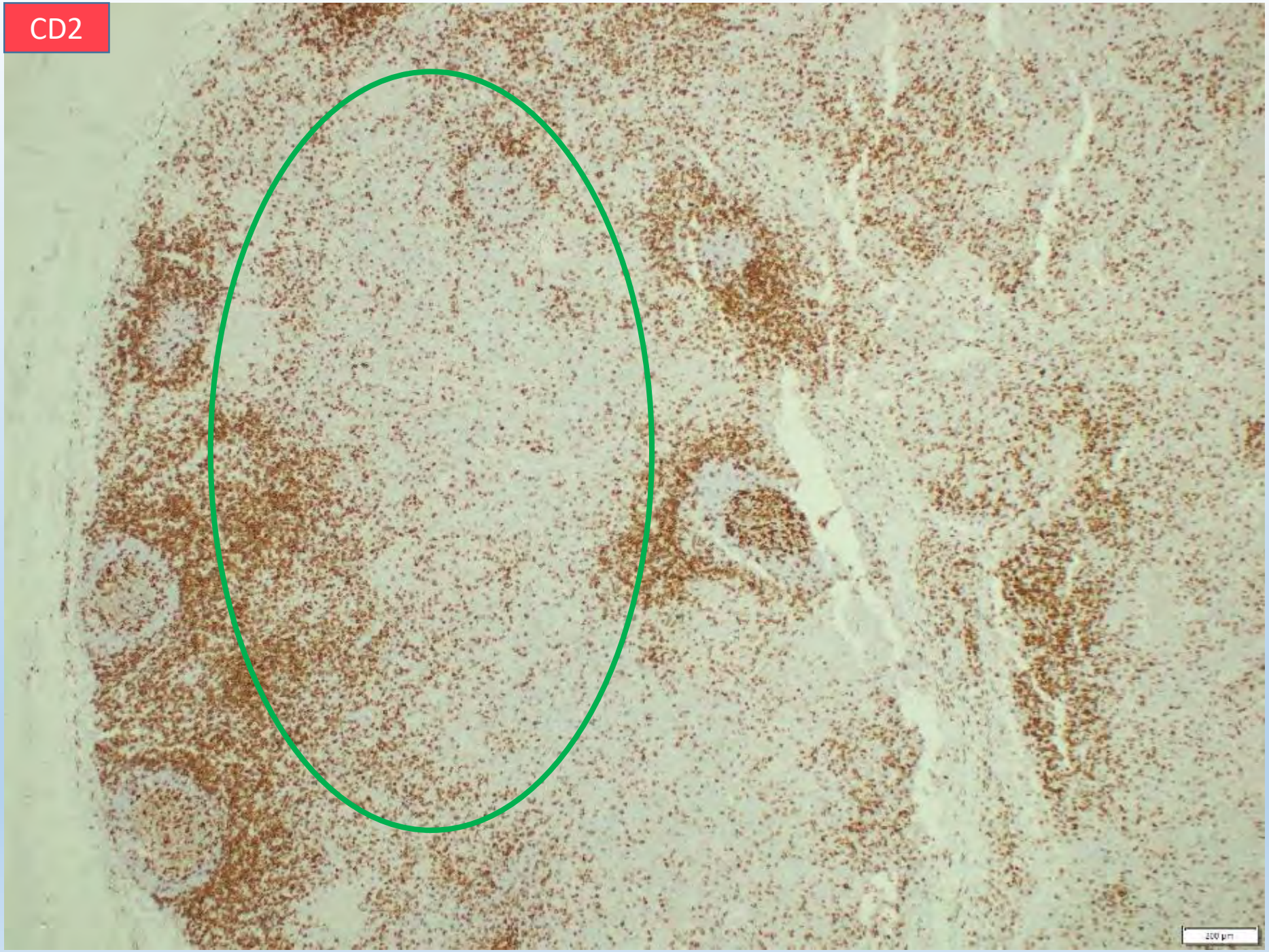

CD20
200 µm


CD3
200 µm

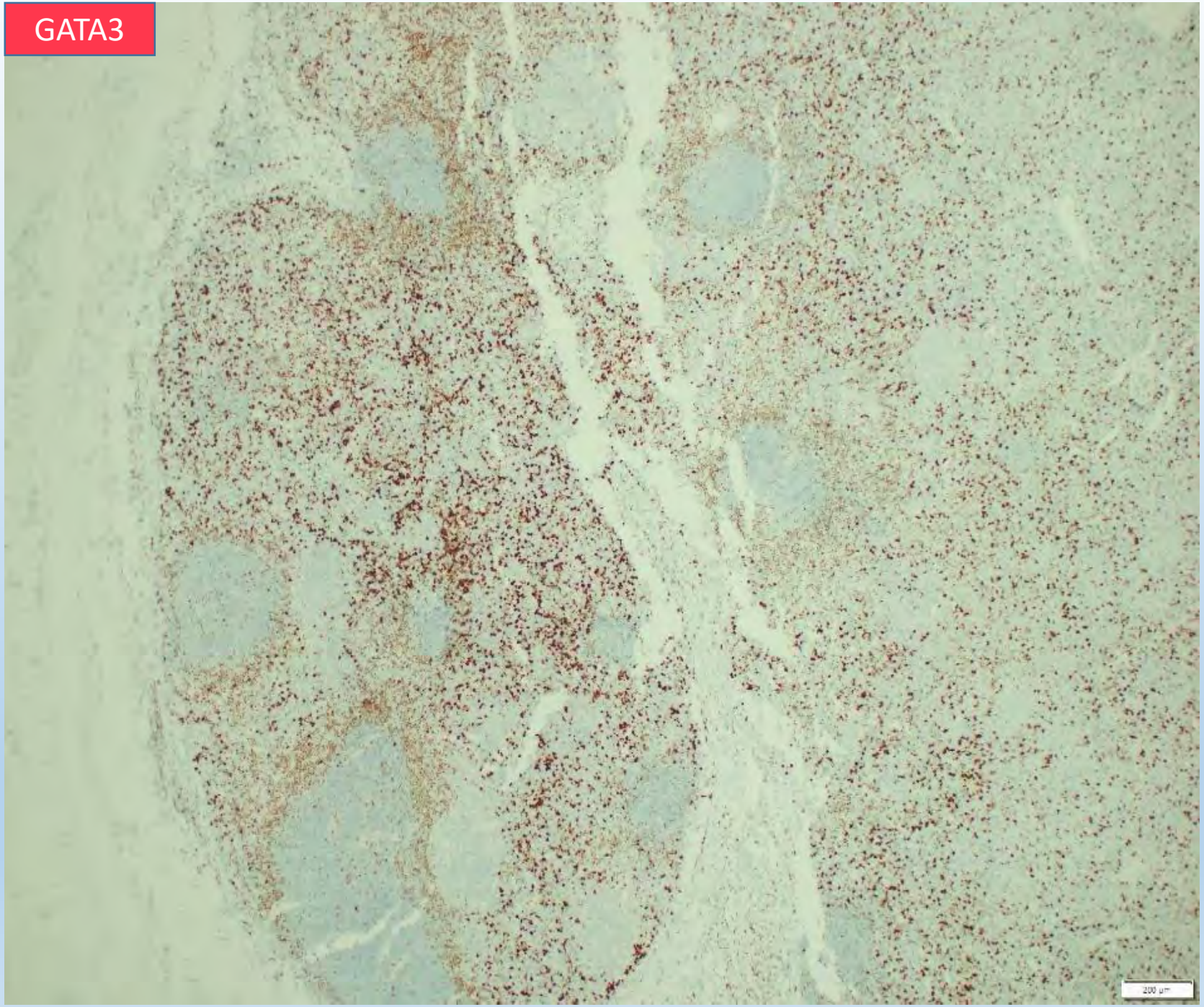

CD4
200 µm


CD5
200 µm

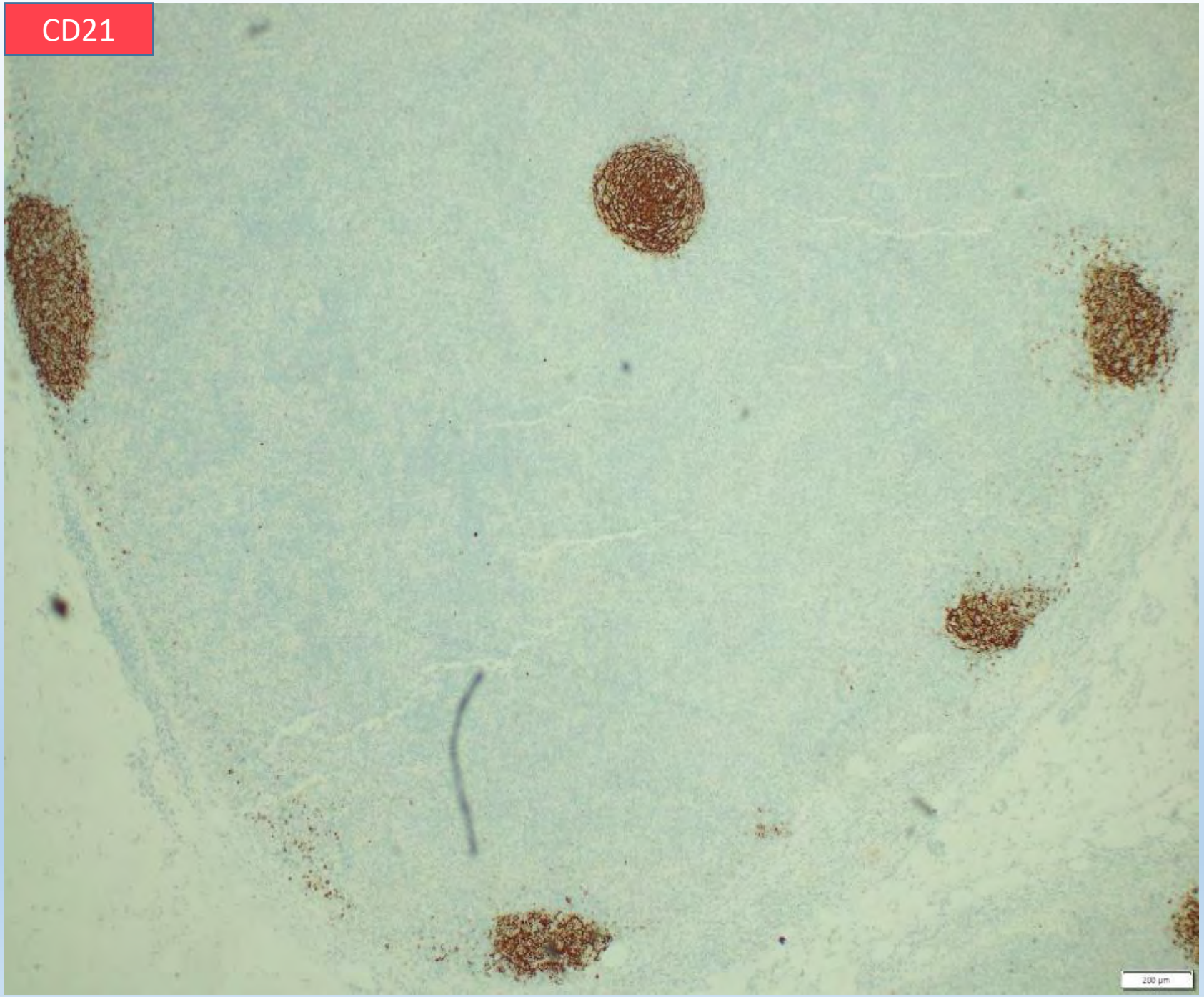

CD7
200 µm


CD2

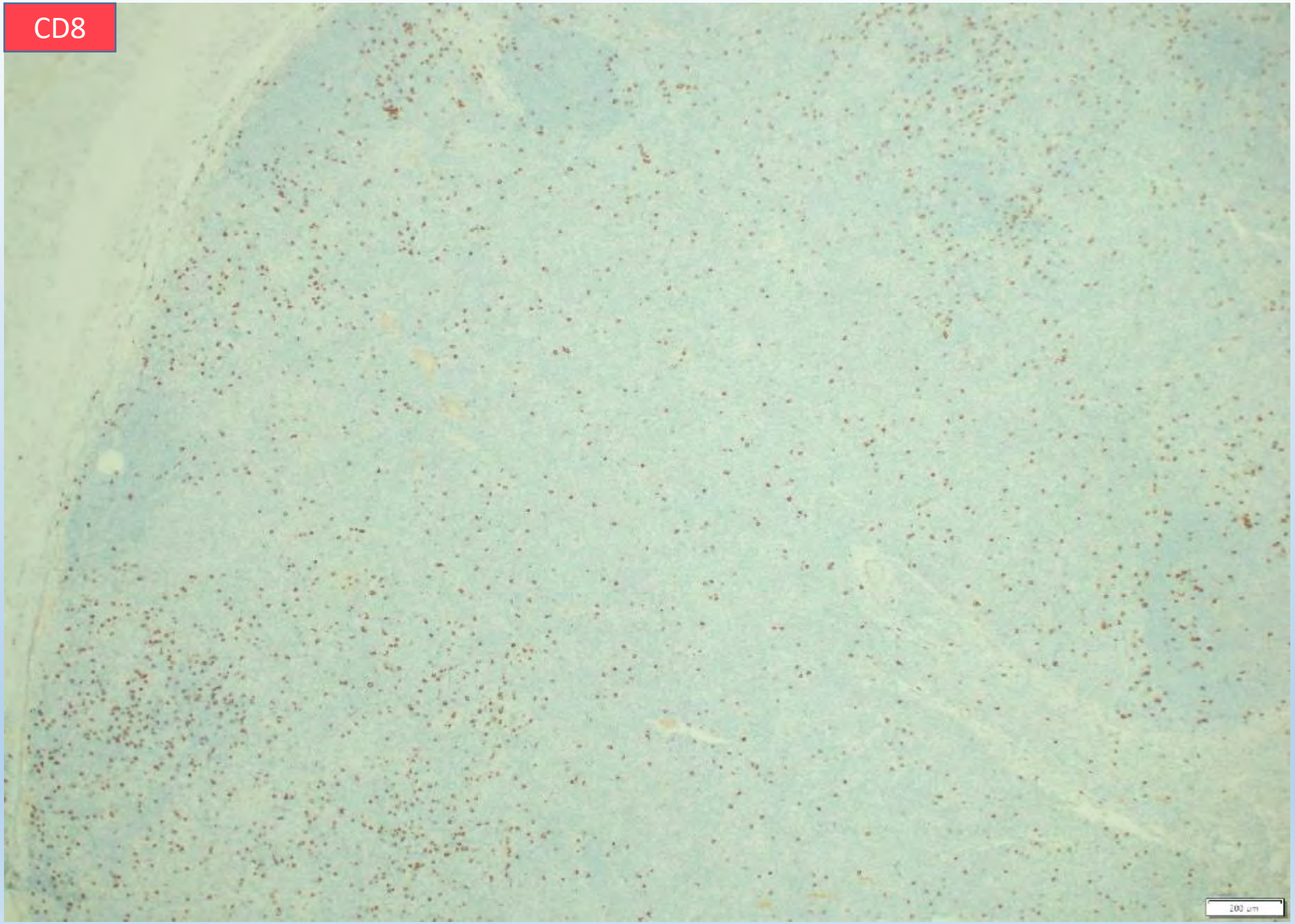
GATA3



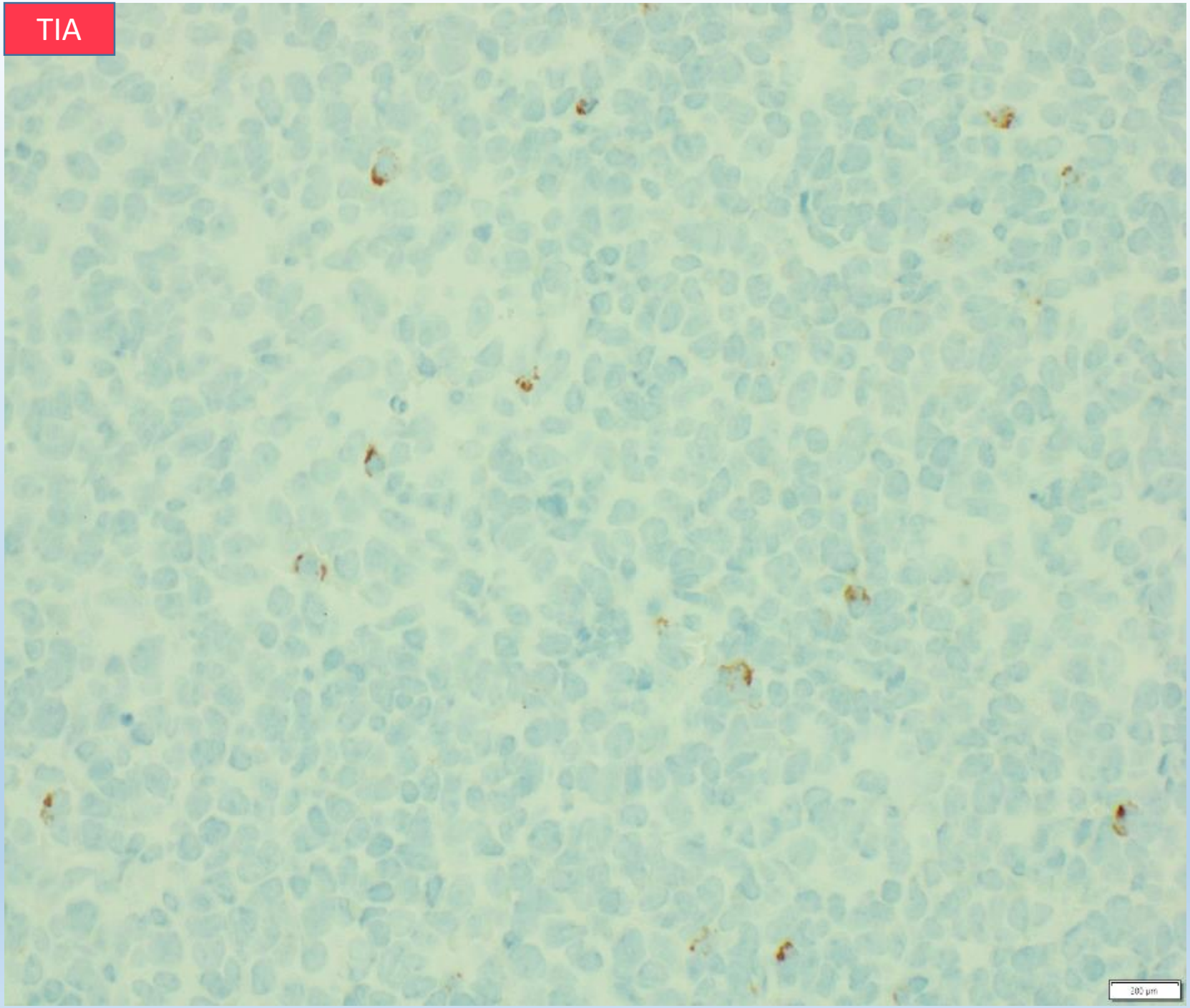
CD21



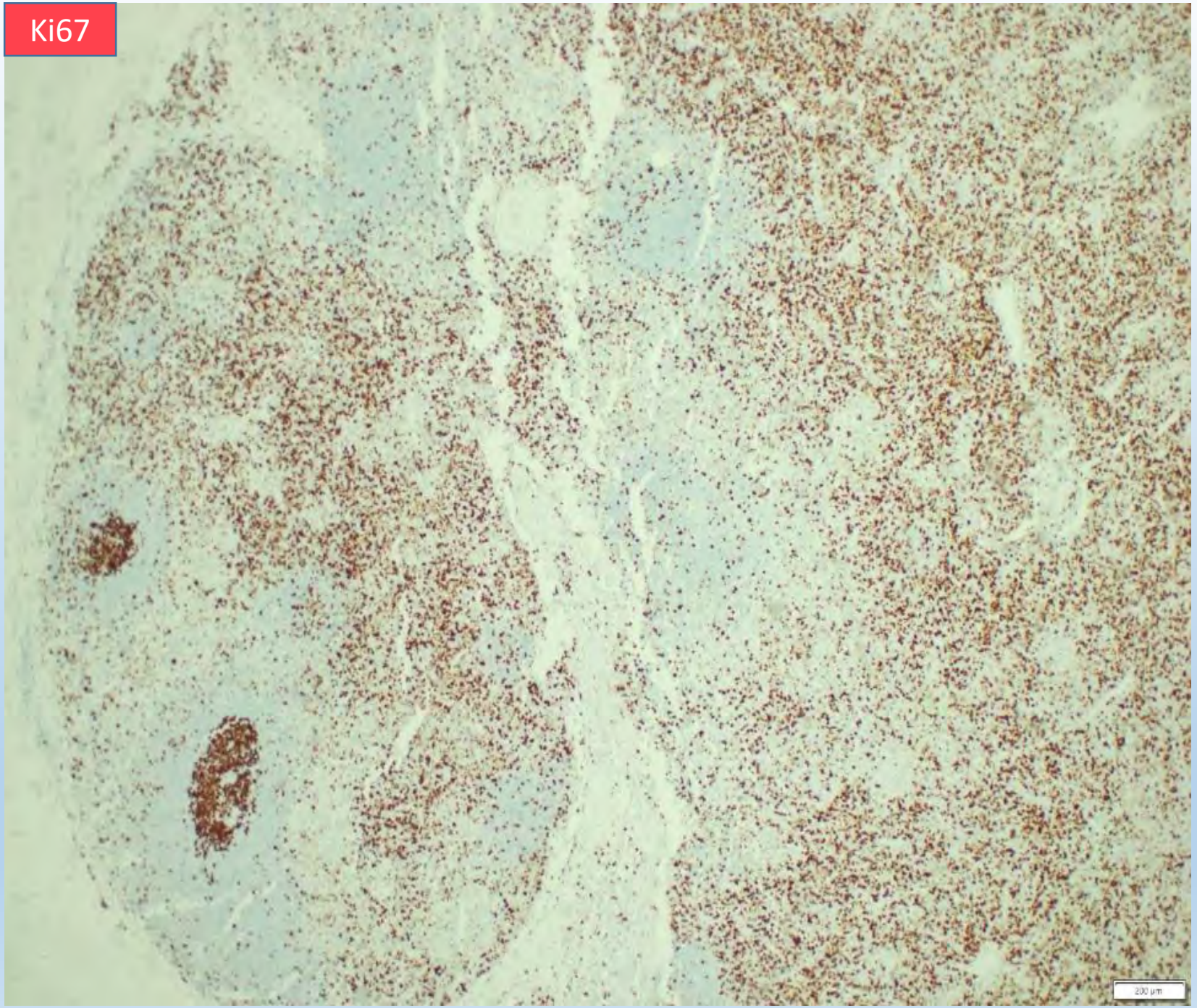
CD8



TIA



Ki67



Diagnosis ??

Peripheral T-cell lymphoma (PTCL) NOS ?

Chromosomal Microarray Analysis: Right Axillary LN

Loss
2q35q37.3

~22 Mb, 40-60% cells

LRP1B (2q37.1) ,
PDCD1 (2q37.3; PD1),
NFE2L3 (~2q37.2)

Gain
6q22.23q27

42 Mb region;
40 – 60% cells

MYB (6q23),
PLAG1(6q24.3),
HACE1(6q24),
ARID1B (6q25.3)

cnLOH
10q21.3q26.3

Encompassing tumor suppressor PTEN and FGFR2

Cytogenomics

Specimen	Cells	Alterations	Details
Right Axillary Lymph Node	40–60%	**10q cnLOH** (PTEN) (69,635,024-135,424,645)x2 hmz	**~66 Mb** region (10q21.3–q26.3); encompasses PTEN (10q23.31) tumor suppressor as well as FGFR2 (10q26.13)
	40–60%	**2q Loss (partial monosomy)** (220,698,125-243,052,331)x1	**~22 Mb** region (2q35–q37.3); LRP1B (2q37.1) , PDCD1 (2q37.3; PD1), NFE2L3 (~2q37.2)
	40–60%	**6q Gain (partial trisomy)** (128,998,864-170,976,062)x3	**~42 Mb** region (6q22.33–q27) MYB (6q23), PLAG1(6q24.3), HACE1(6q24), ARID1B (6q25.3)

Right axillary LN - NGS (275-gene panel)

Gene	Protein Change	cDNA Change	VAF (%)	Exon	Clinical Tier
TET2	p.Asn275fs	c.822delC	35.7	3	Tier 2 frameshift p.N275fs*18
TET2	p.Gly1370Glu	c.4109G>A	31.8	9	Tier 2 missense p.G1370E
DNMT3A	p.Gly413fs	c.1238delG	32.1	10	Tier 2 frameshift p.G413Afs*23 8
DNMT3A	splice_donor	c.1667+1_1667+2insA	33.6	14	Tier 2 (splice donor ins
CEBPA	p.Gly242Ser	c.724G>A	54.5	3	VUS/ likely pathogenic
SOCS1	p.Arg20Leu	c.59G>T	53.4	2	VUS Missense p.R20L
NRAS	p.Gly13Arg	c.37G>C	9.3	2	Tier 2 Hotspot mutation (G13R)

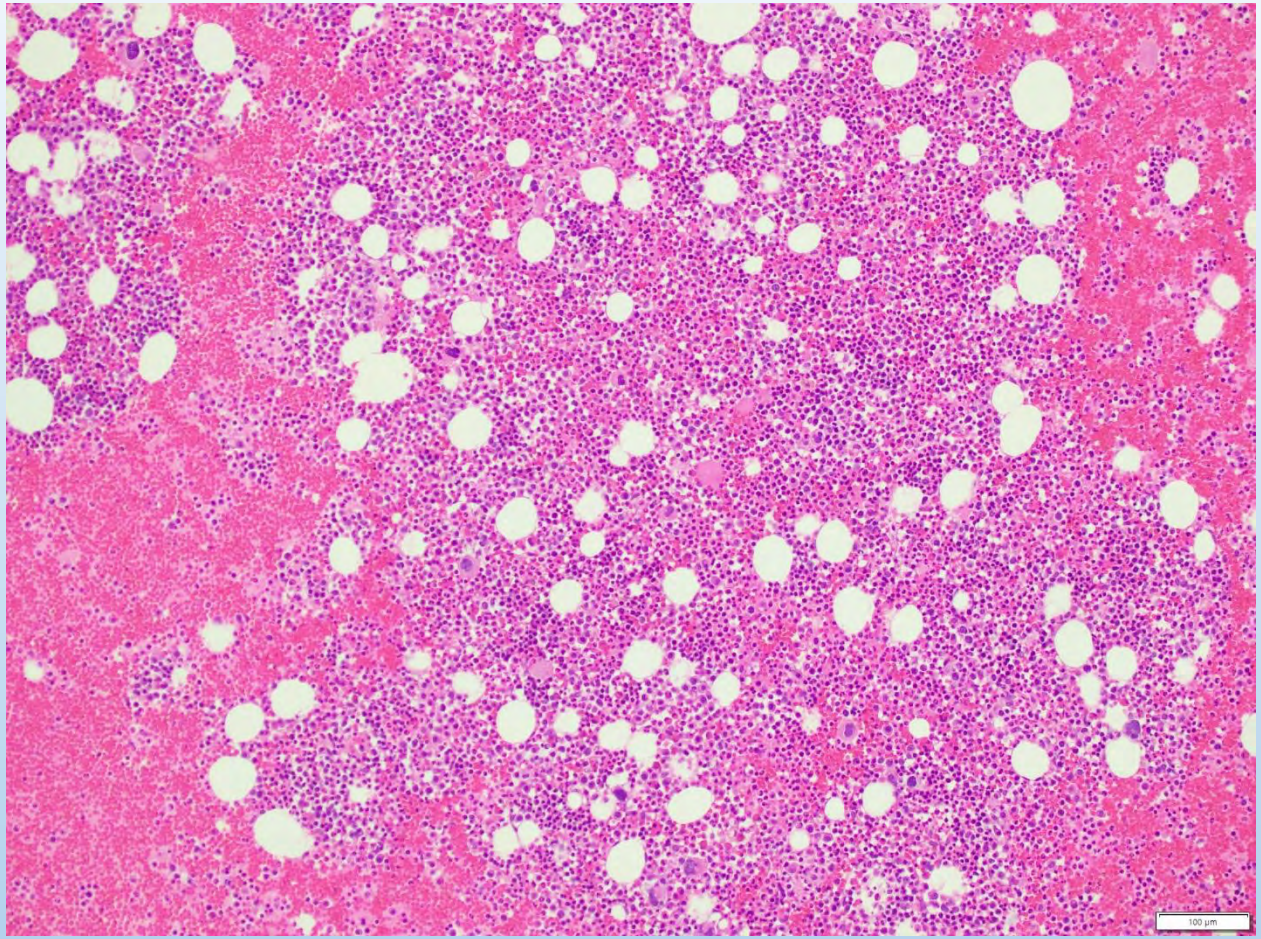
Right axillary LN: T Cell Clonality

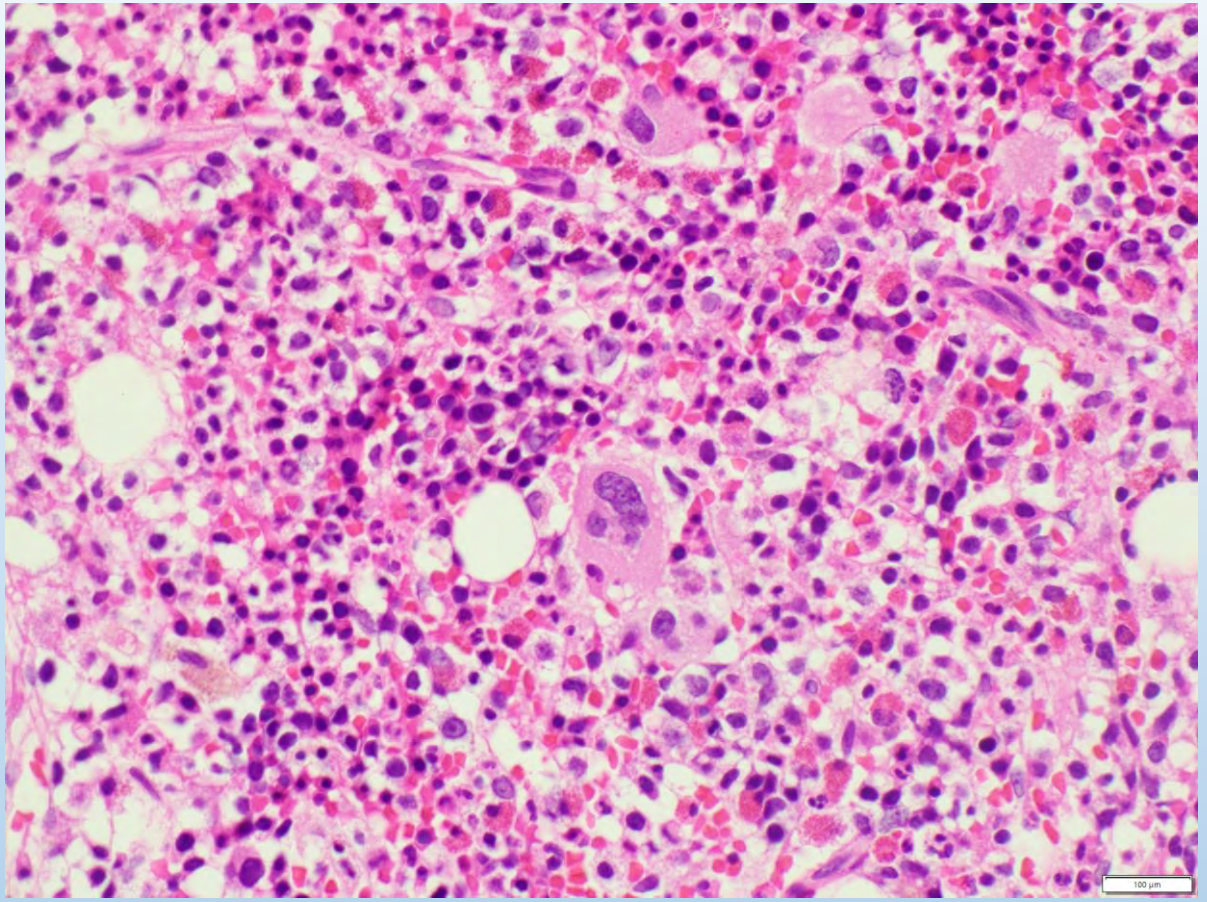
T-cell Receptor Beta gene rearrangement :
Positive

Right axillary LN: RNA Fusion Panel

No fusions detected

Staging Bone marrow





Hypercellular (70–80%), maturing trilineage hematopoiesis<1% blasts,

Flow:

Low-level aberrant T-cells (~1.5% total, CD3-/CD4-)

Summary

- ✓ Multi-station lymphadenopathy
- ✓ Morphology
- ✓ Aberrant maturing T-cells (flow)
- ✓ Partial T-antigen loss (by IHC)
- ✓ Tier 2 TET2 LoF variants
- ✓ Tier 2 DNMT3A mutations (×2)
- ✓ PTEN loss
- ✓ T-cell receptor beta gene rearrangement : Positive

Diagnosis

Peripheral T-cell lymphoma (PTCL) NOS

Follow up after 8 weeks (s/p C2 CHOP Full dose

Re-demonstration of

- Bilateral axillary lymphadenopathy, with interval mild enlargement in some nodes, including left supraclavicular lymph node (Level IV). Other nodes: Stable or partially regressed.
- Extensive bulky abdominopelvic lymphadenopathy, with some lymph nodes slightly interval increased in size compared to prior.

Left Cervical core biopsy

- Diffuse infiltrate of atypical medium to large sized atypical cells
- Necrosis is absent.
- Mitotic activity is low.

Left Cervical core biopsy

Immature neoplastic cells positive for T-cell lineage markers:

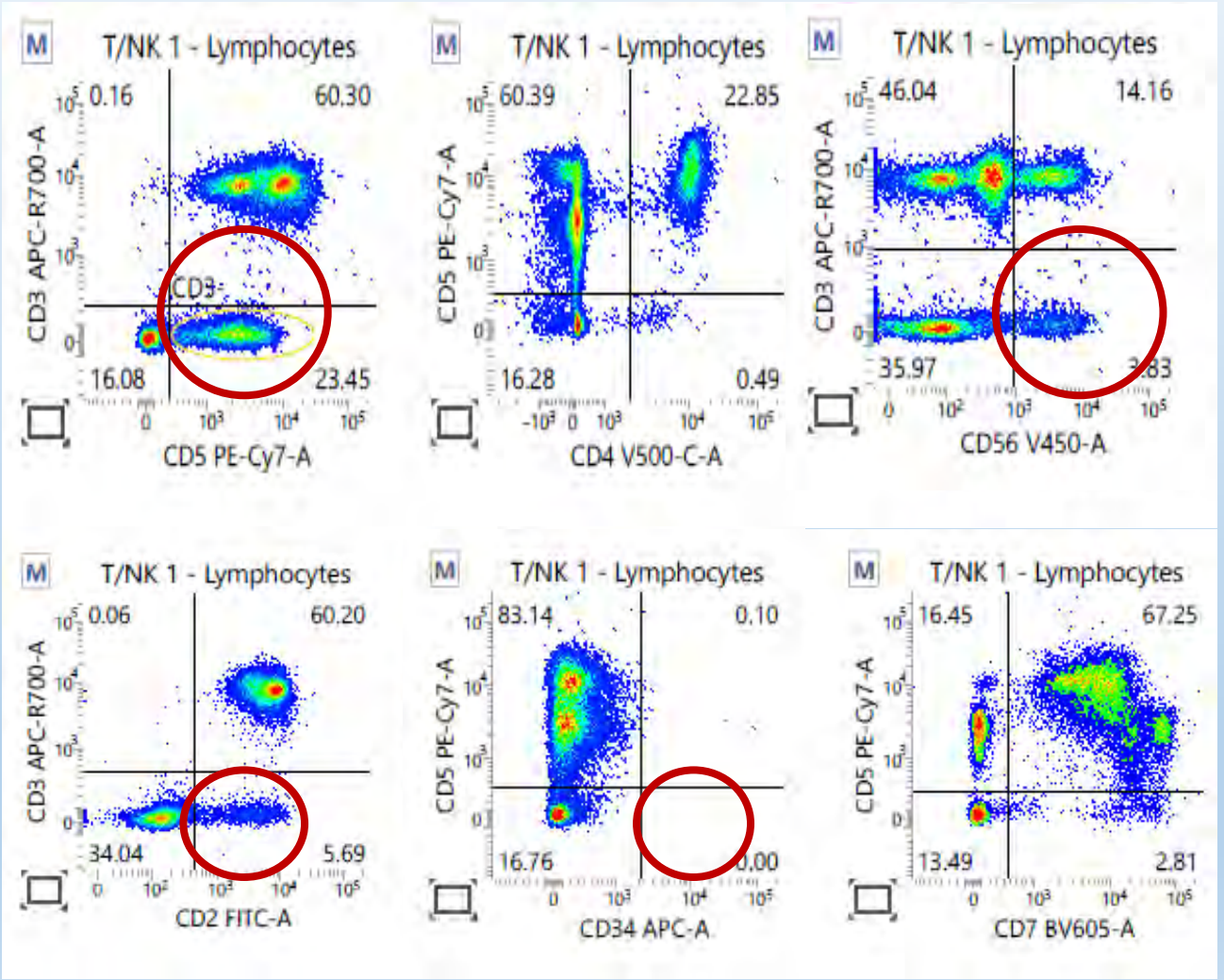
CD3 (weak, small subset), CD4, CD2 (weak, small subset), CD5 (weak, subset), CD7, CD34, and TdT. These cells are negative for CD8, CD10, CD56, CD123, BCL6, and TCL1.

In the background, there is also an abnormal maturing T-cell population positive for CD4, CD2 (weak, small subset), CD5 (weak, subset), CD7, and negative for CD8, CD34, TdT, and TCL1.

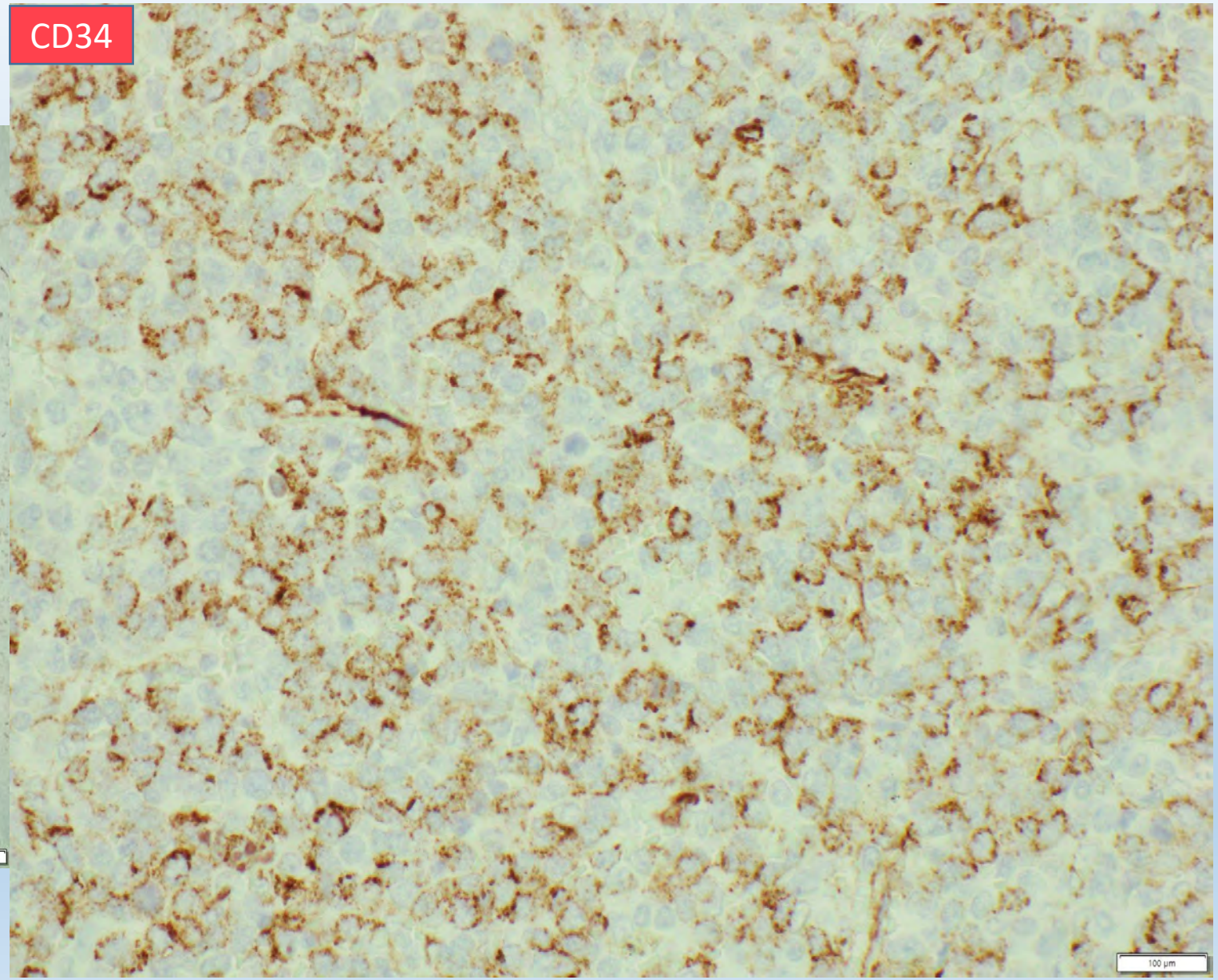
Peripheral blood (Late Nov 2025)

An abnormal lymphocyte population is detected (23% of lymphocytes):

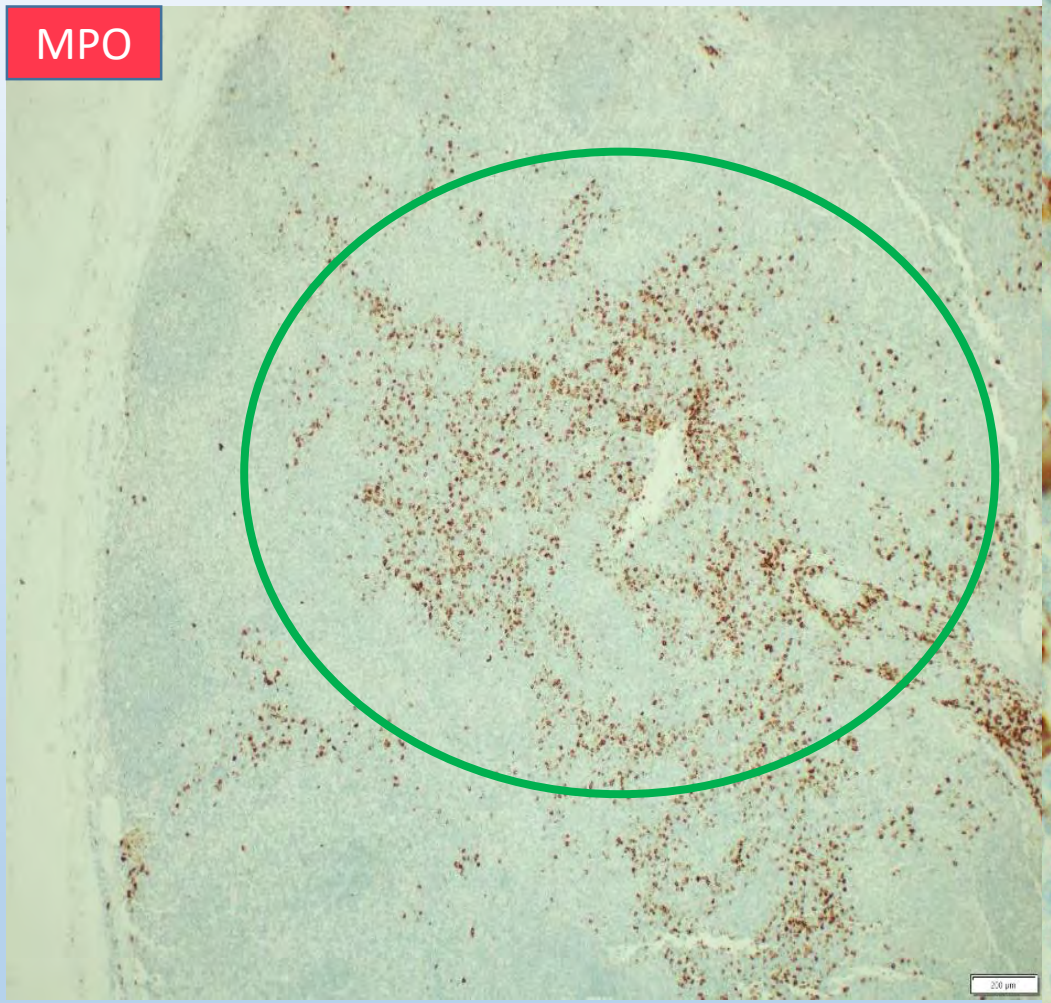
CD5+, CD7+, CD33 dim/partial+, CD56 partial+, CD2-/+, CD3-, CD4+, CD8-, CD10-, CD34-, TdT-.



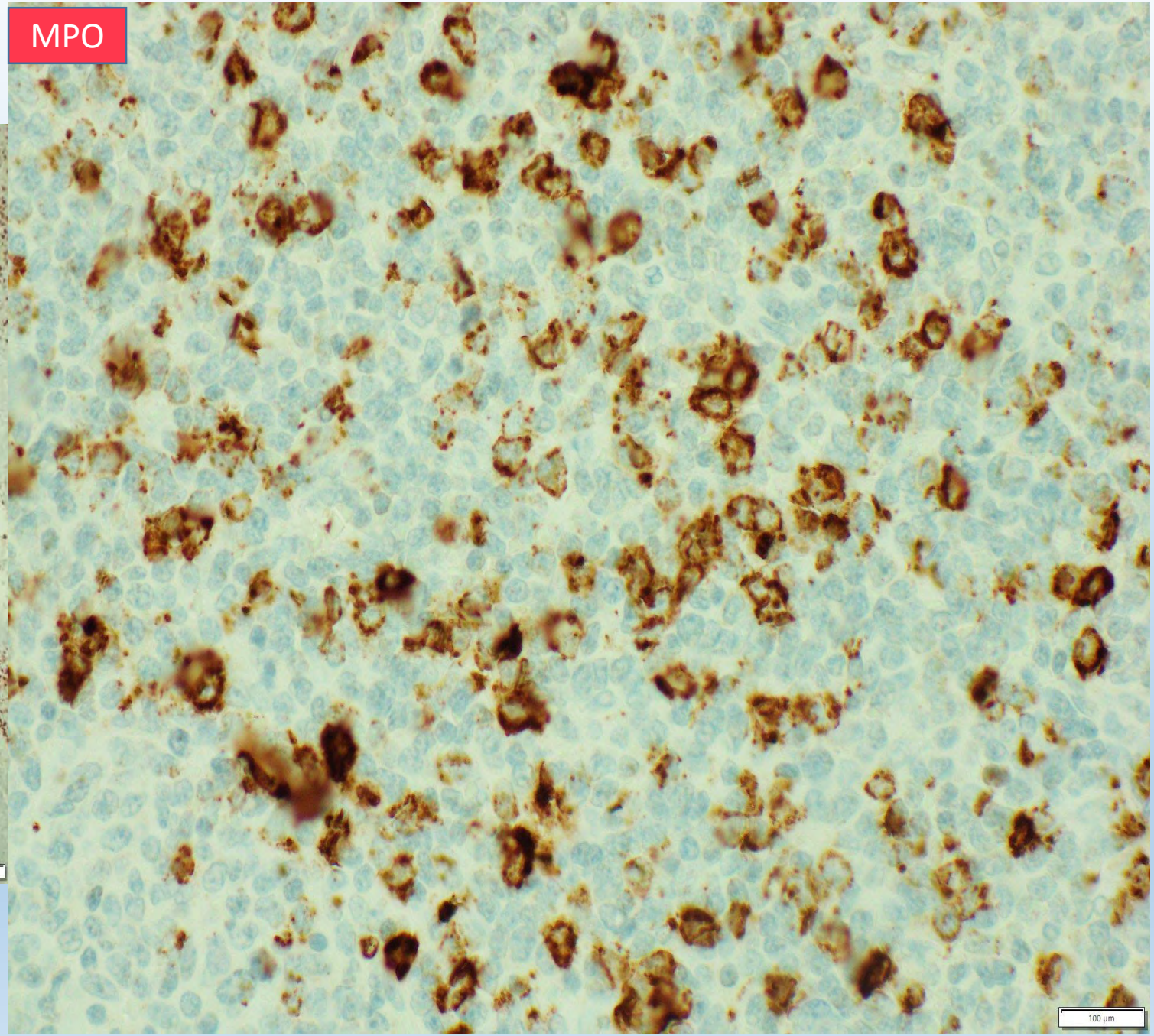
Right axillary LN (Re-review: Original)

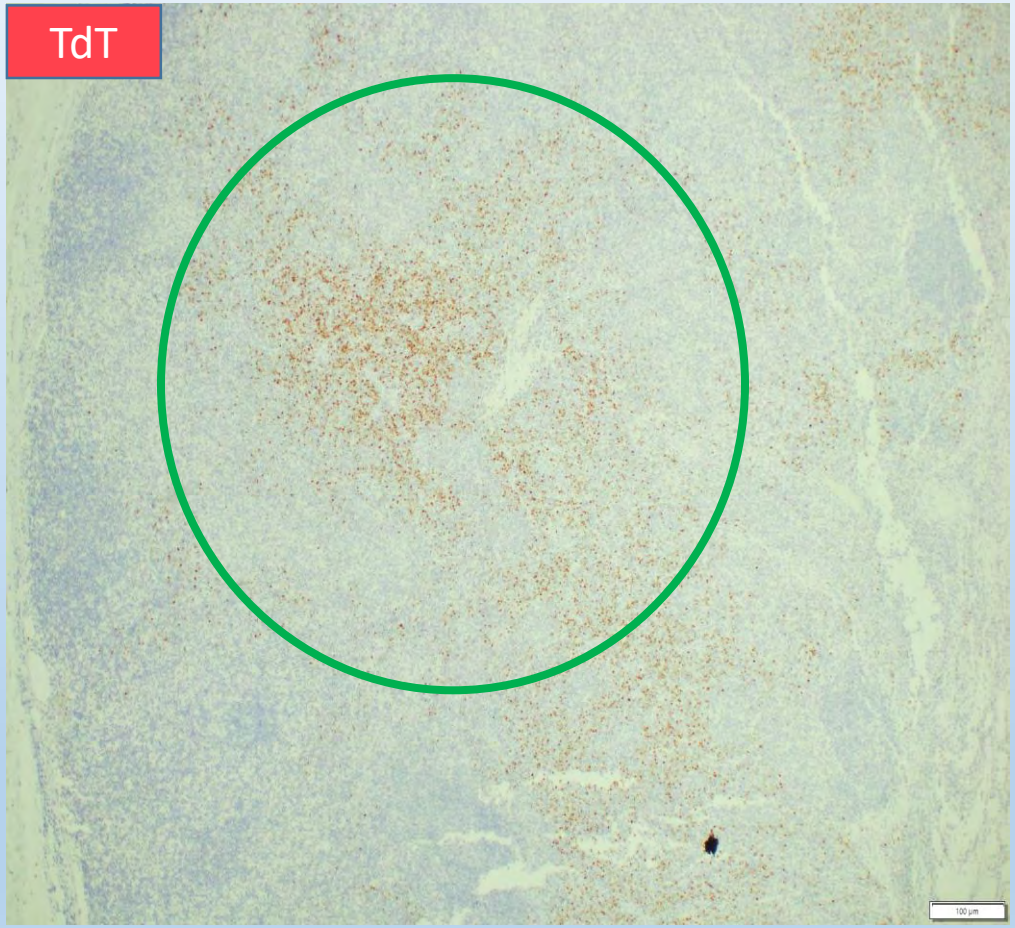


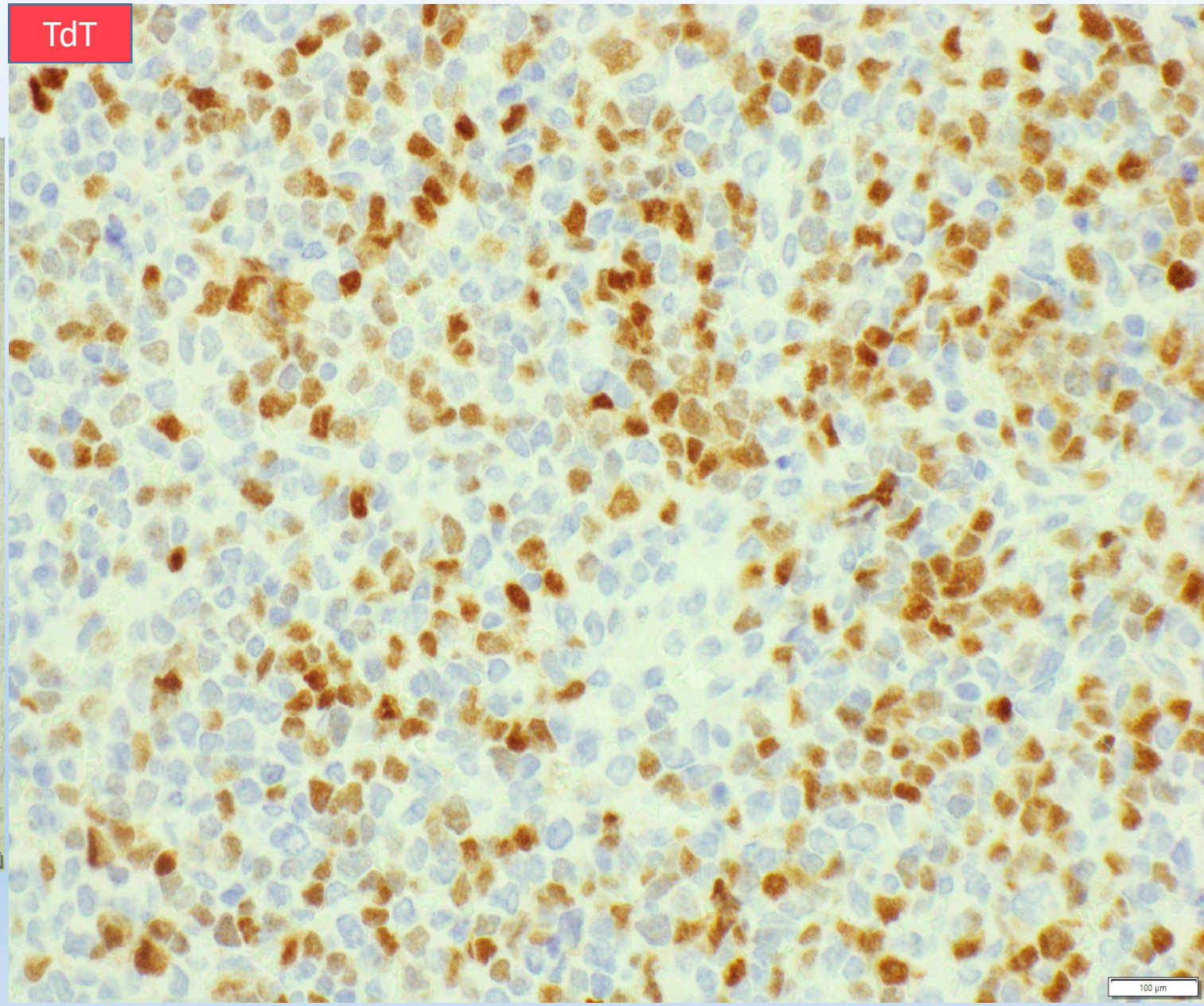
MPO



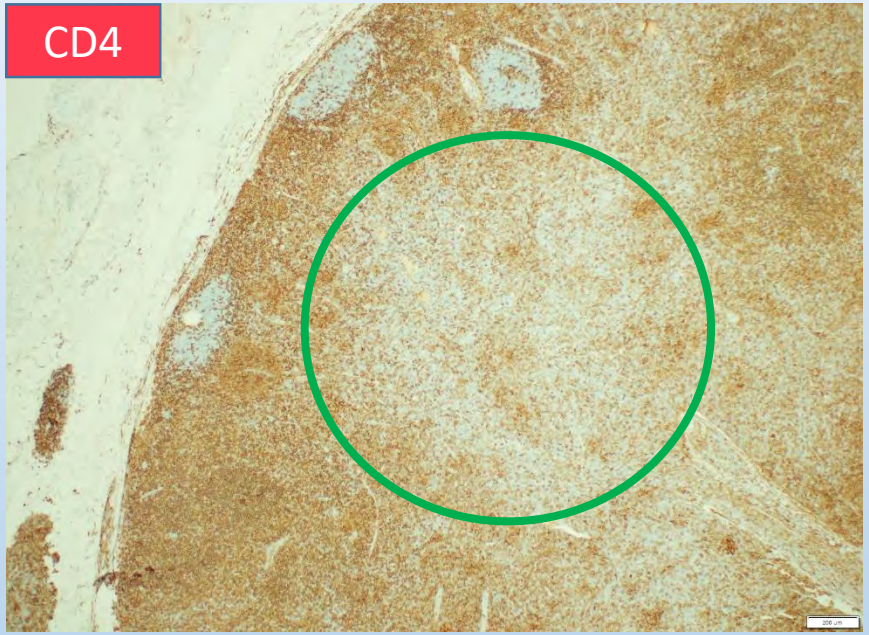
MPO



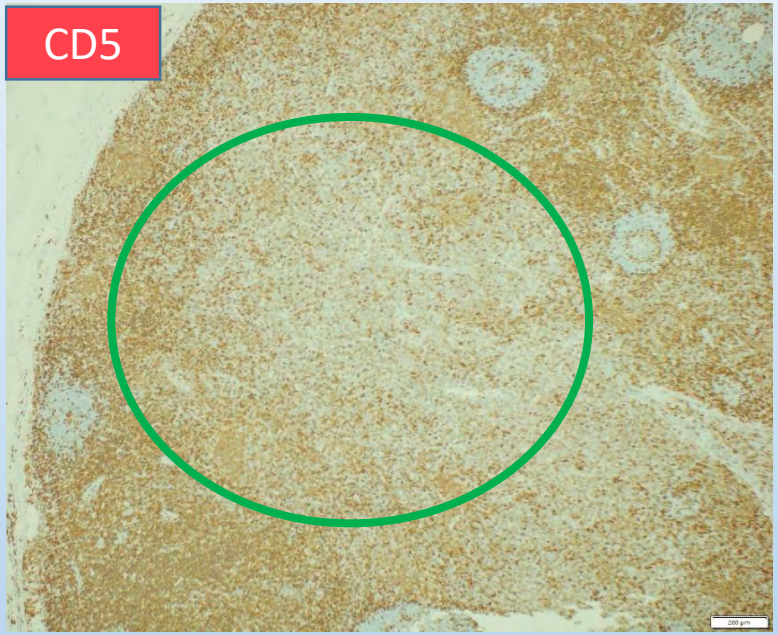

TdT


TdT
100 µm

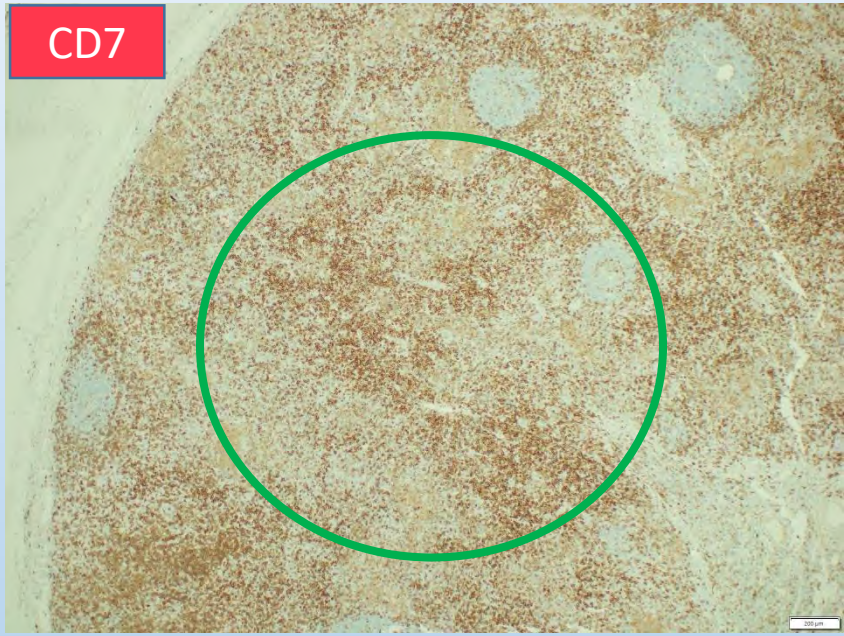
CD4



CD5

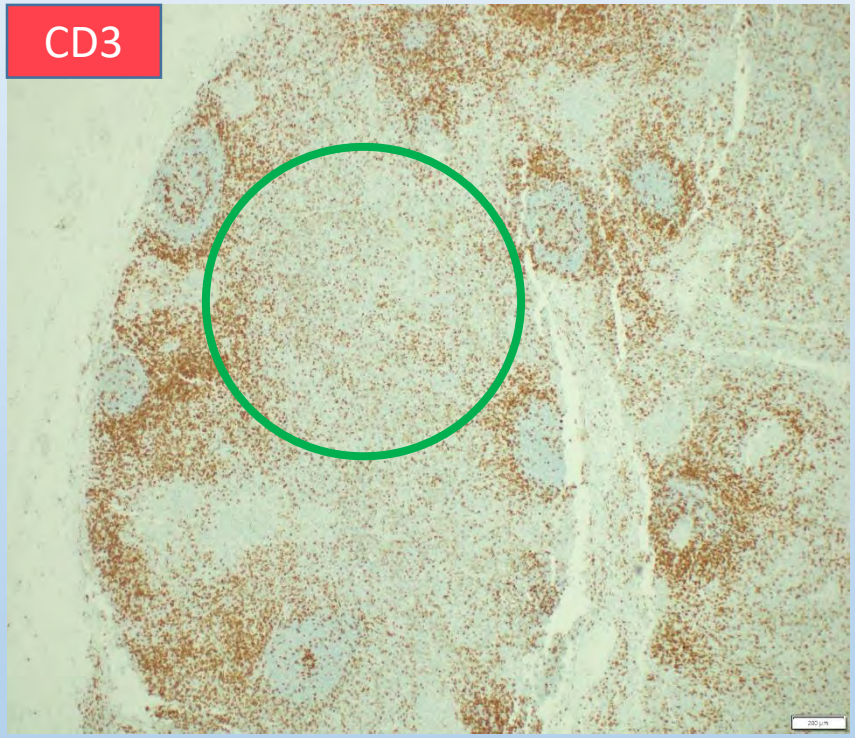


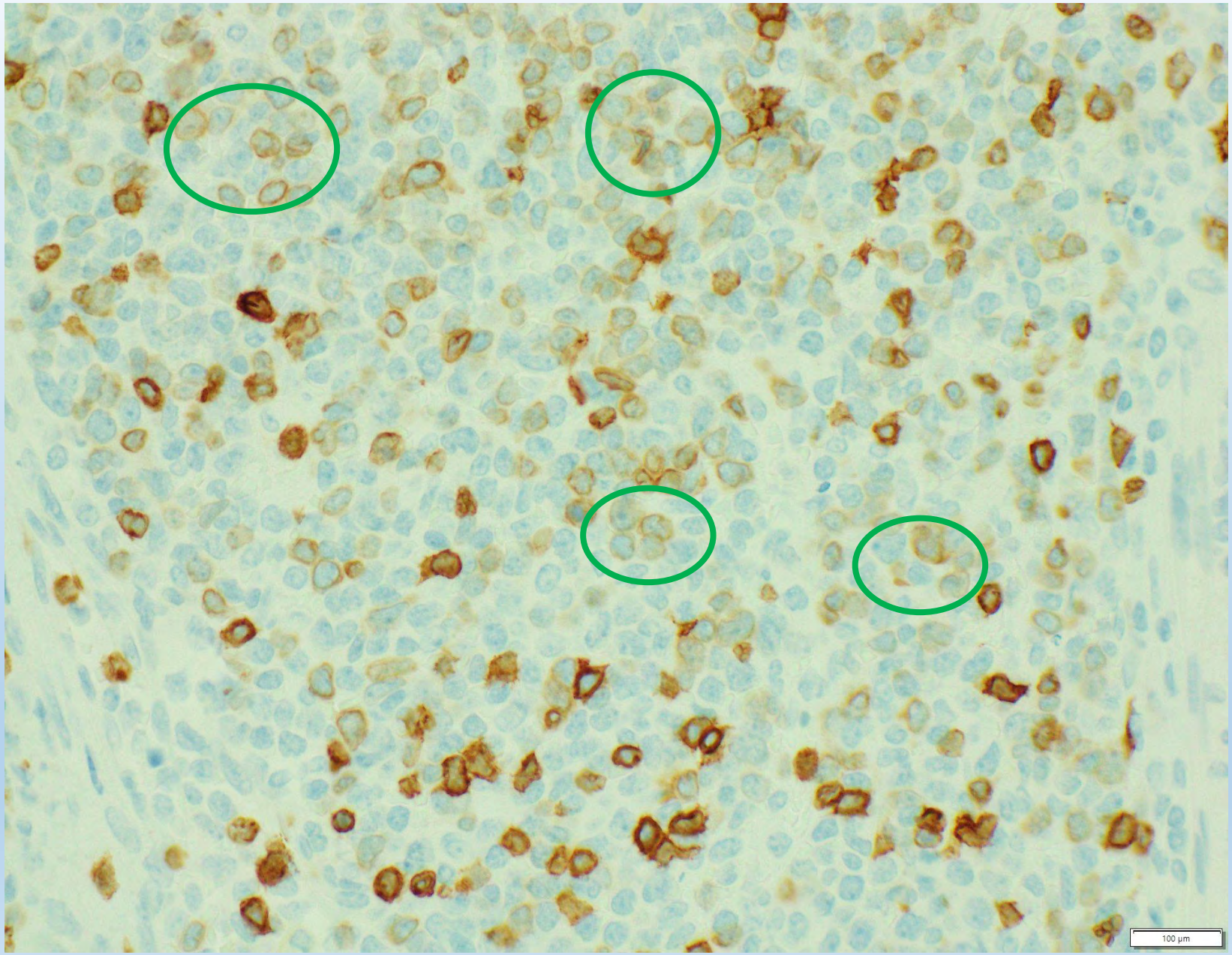
CD7



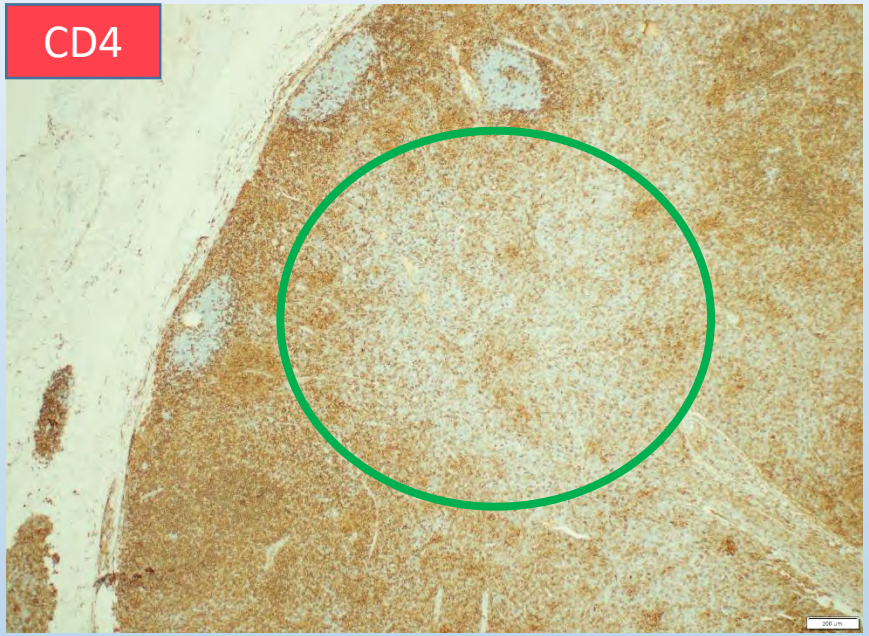
CD4 Predominance with aberrant CD5 and CD7

CD3

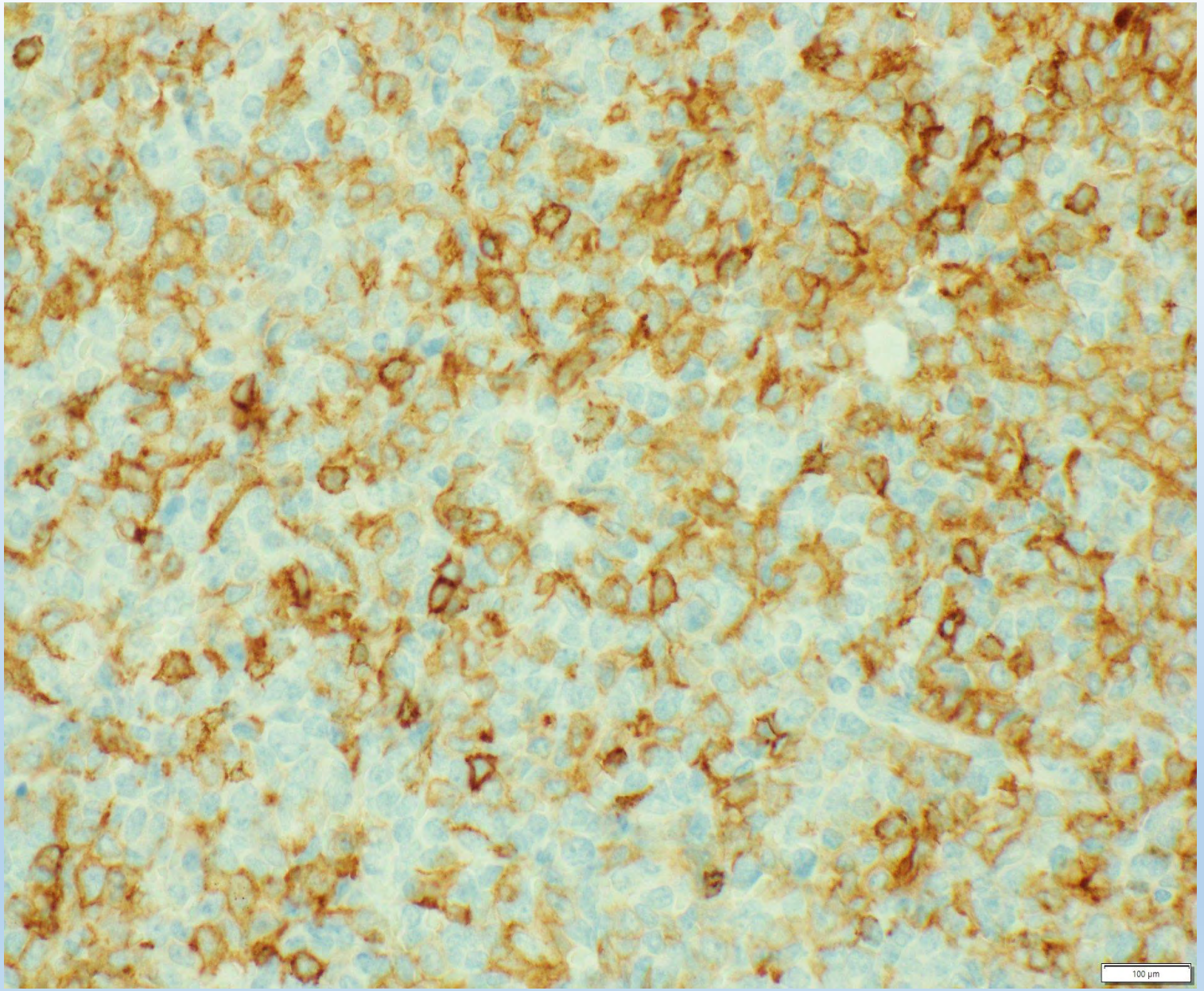




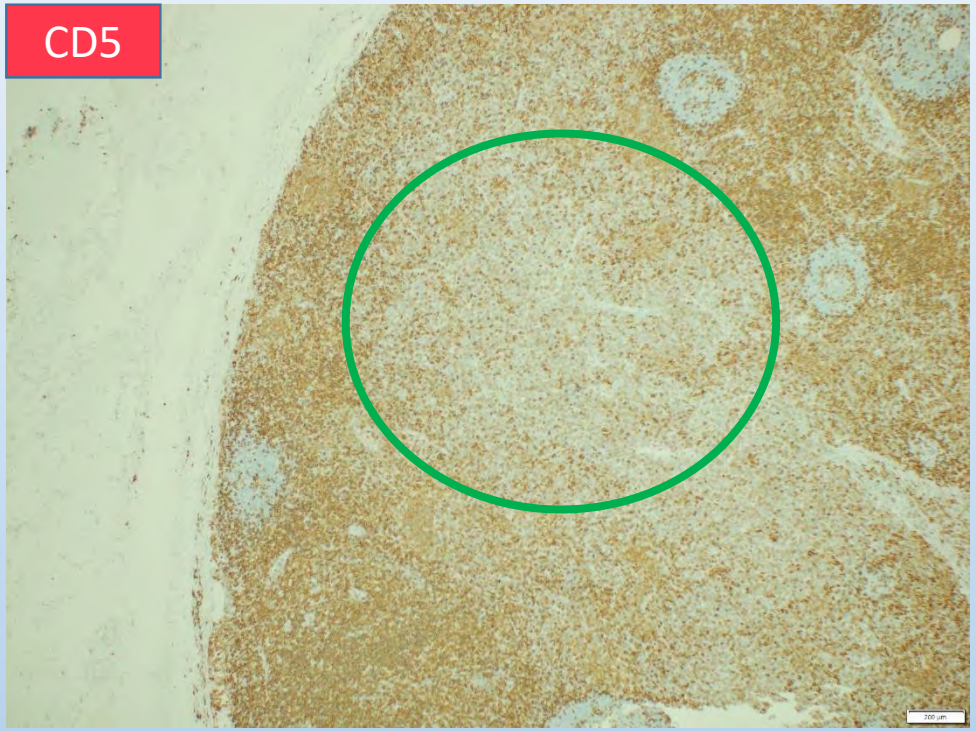
CD4

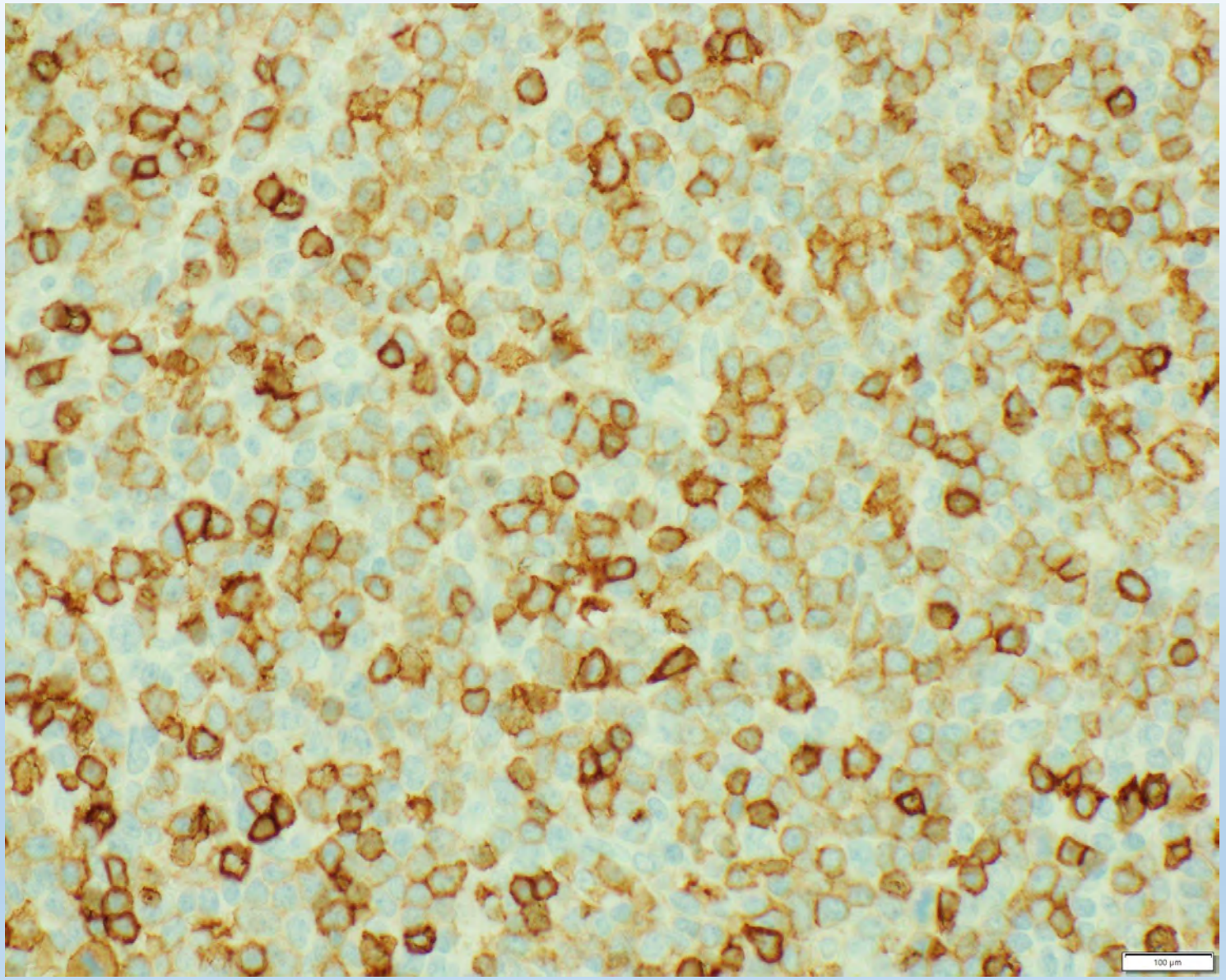


CD4 (weak)

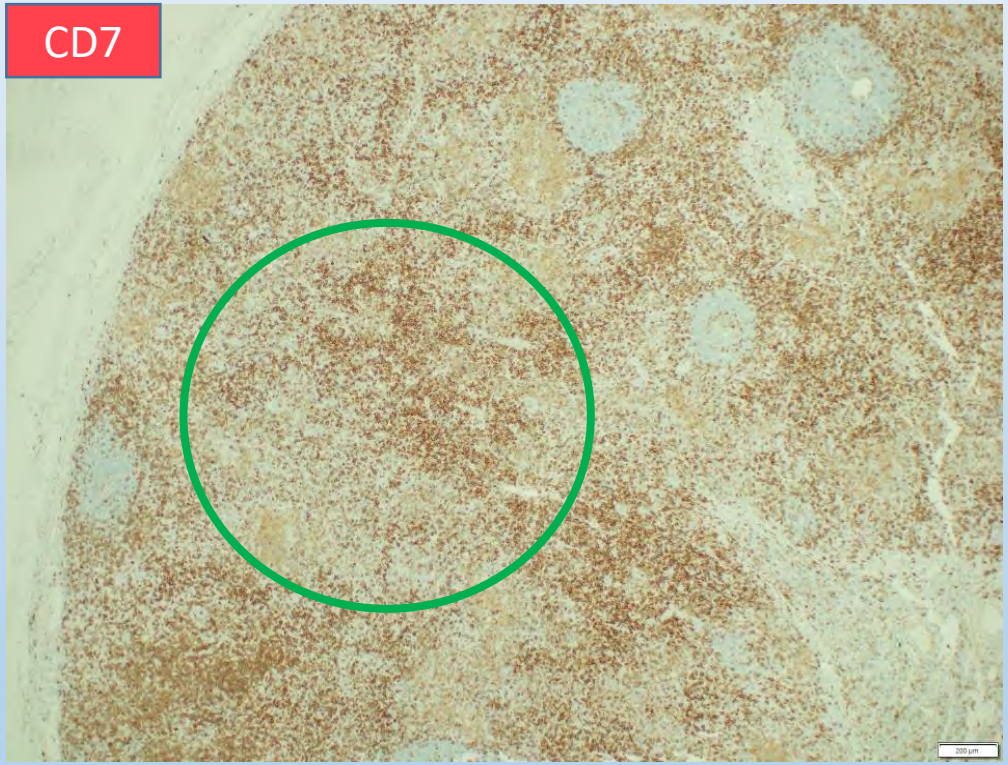


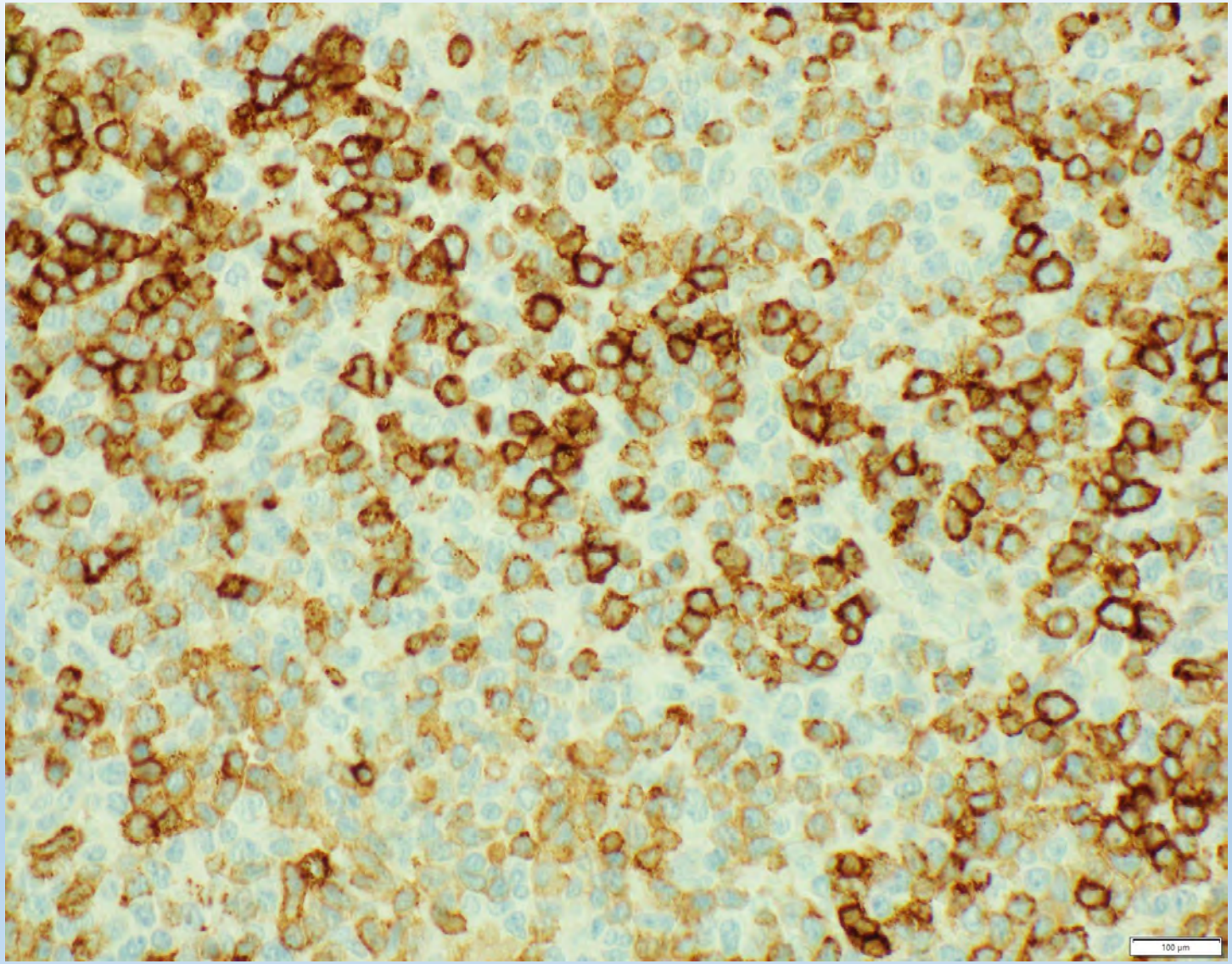
CD5

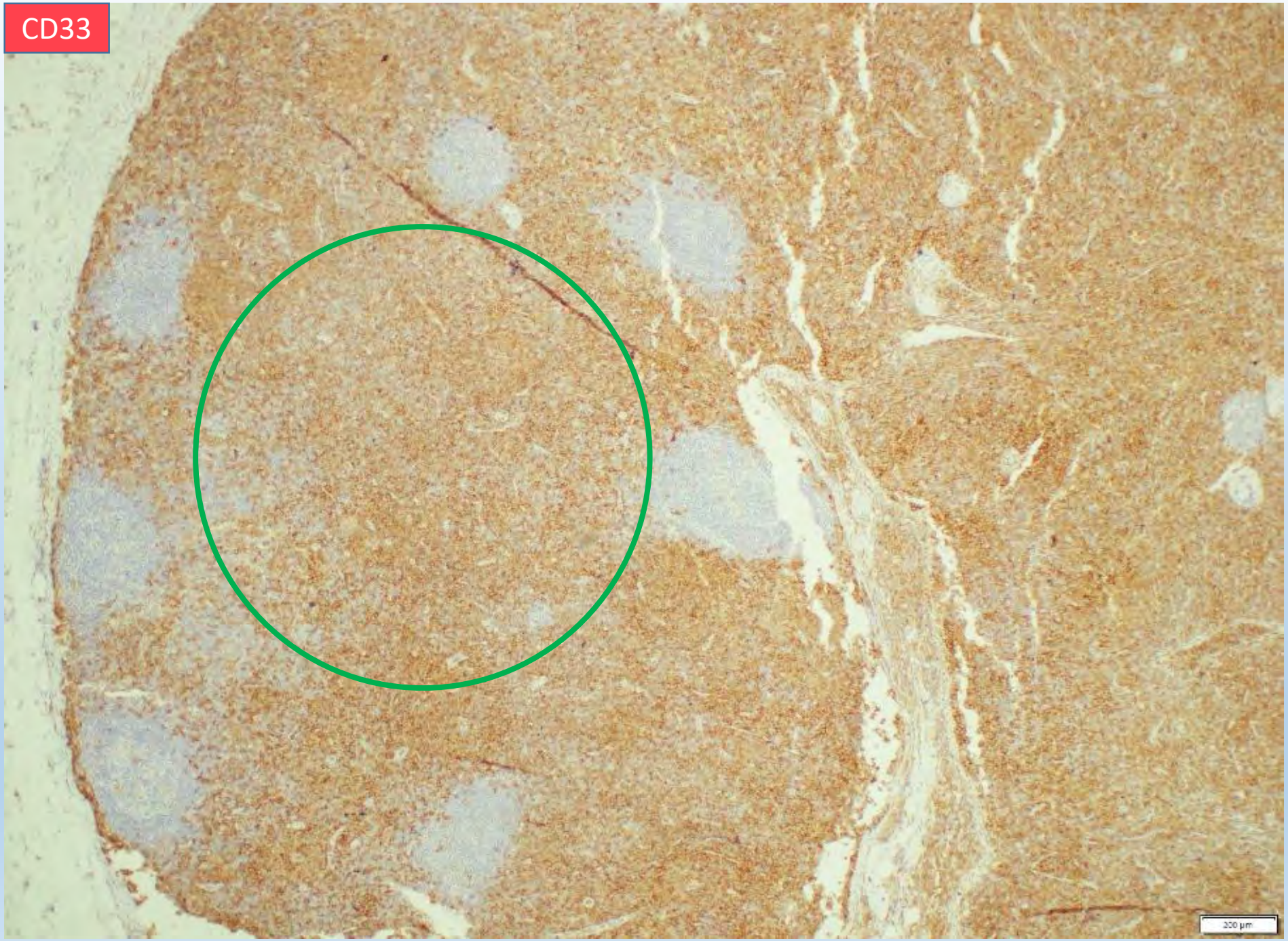


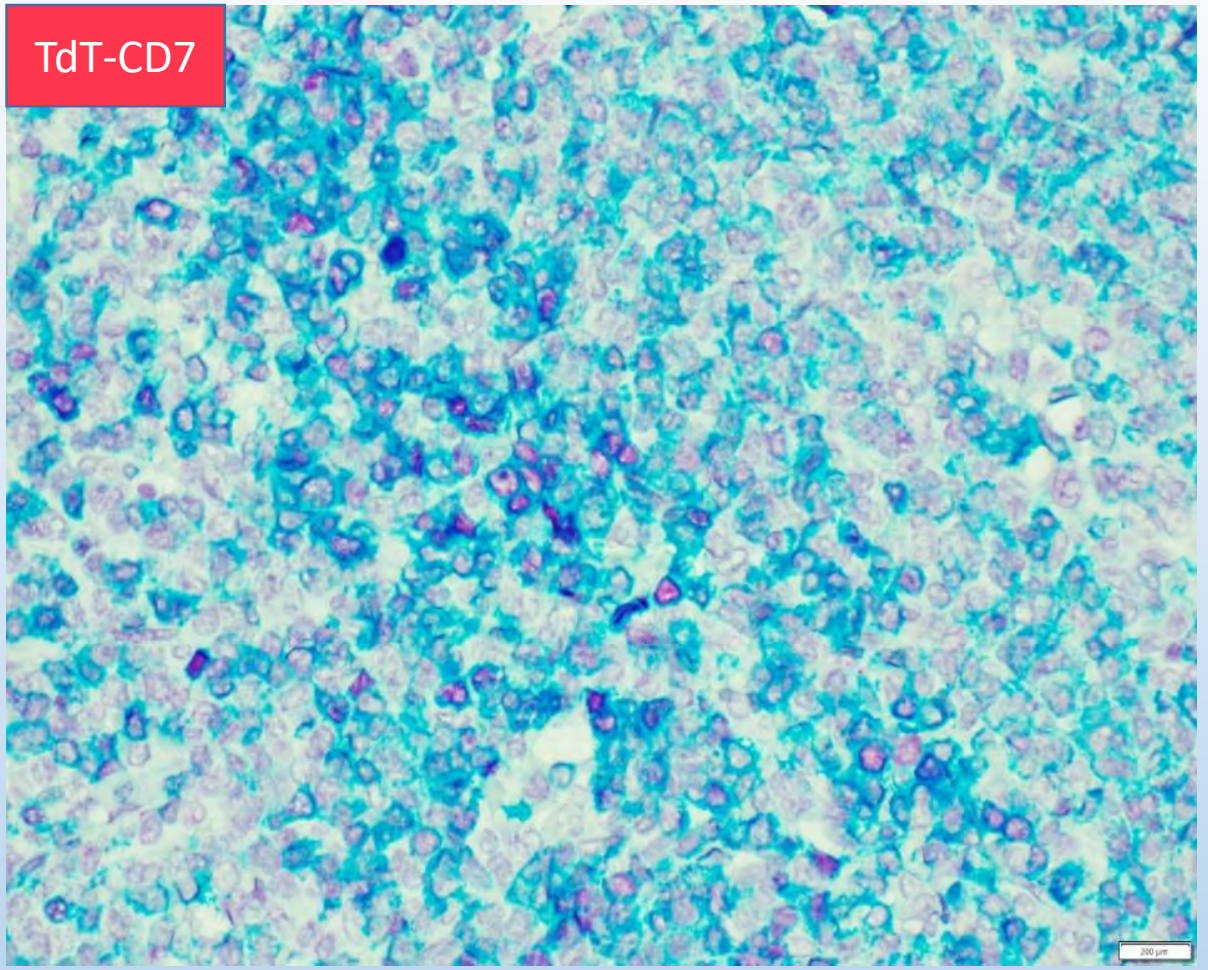


CD7





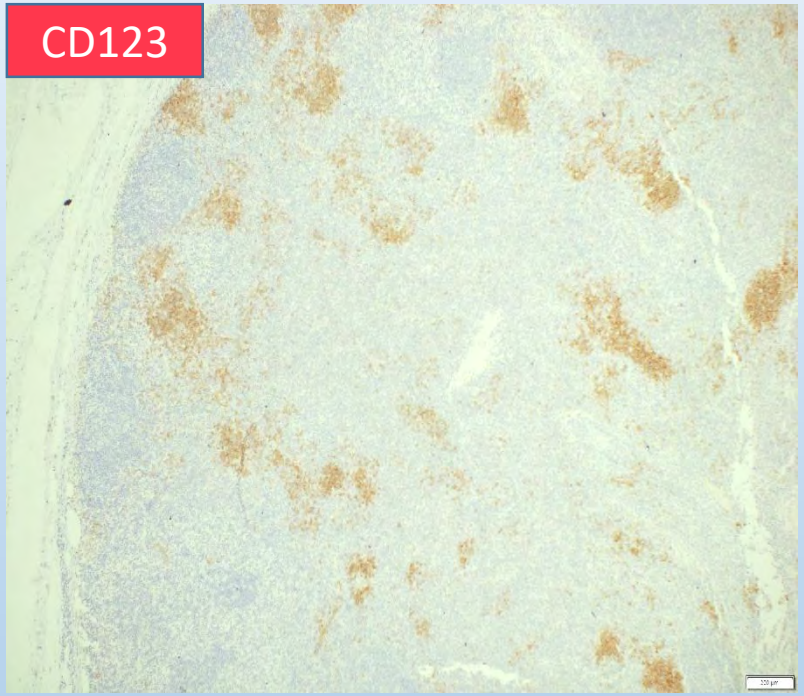

CD33
200 µm



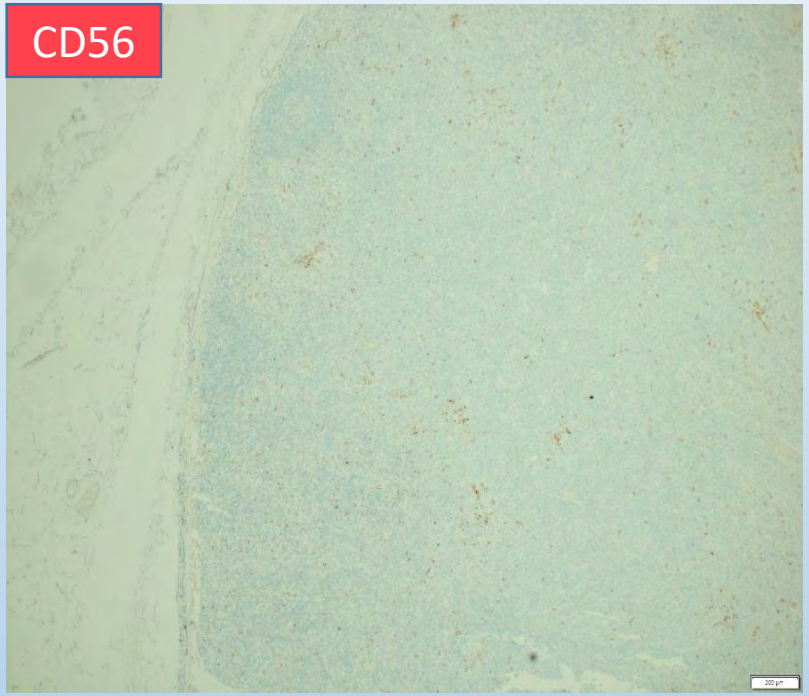
CD99: Immature marker supporting CD34/TdT

TdT-CD7 coexpression:
CD7 : Earliest marker of T-cell development

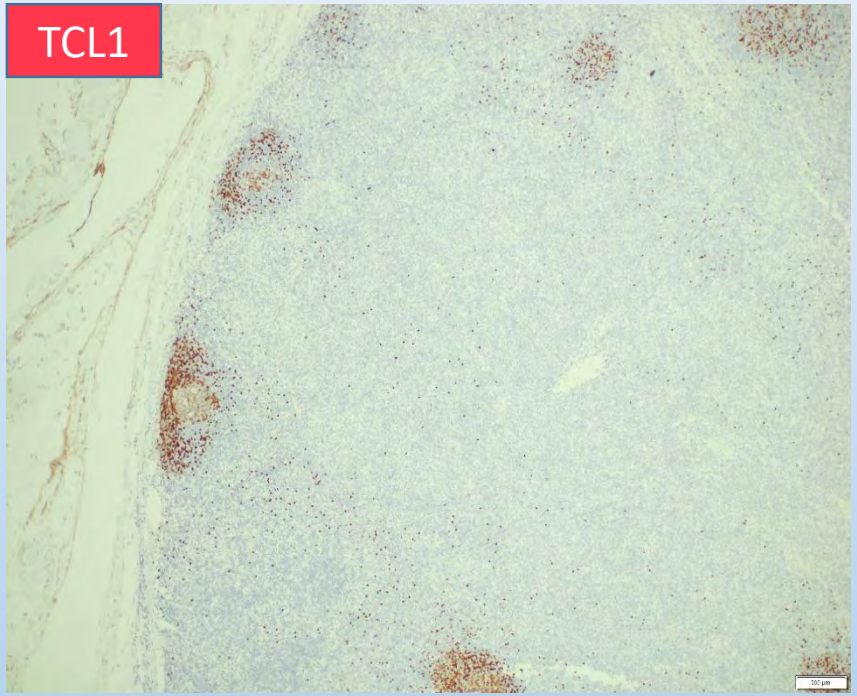
CD123



CD56



TCL1



CD123+/CD303+/CD4+/CD7+
Plasmacytoid dendric cells aggregates;
can be seen in TFH-derived lymphoma

Both CD56 and TCL-1 negativity is rare

TCL-1 highlights follicular B-cells

IHC summary

Cell Type	Category	Positive Markers	Negative Markers
Blasts (biphenotypic/bilineal)	T-cell	CD3 (weak; small subset), CD4 (weak; partial), CD5 (weak), CD2 (small subset), CD7+	CD8-, CD1a-
	Myeloid/Stem	TdT+, CD33 (diffuse)+, CD34 (partial), CD99+, MPO (partial)+, Lysozyme+, Dual TdT and CD7 coexpression	CD117(mostly negative); rare cells-
	B-cell	None	CD20-, PAX5-
	Other	None	CD15-, CD30-, CD123-, CD56-, ALK-, CD21-, CD23-, CXCL13-, ICOS-, PD1-, EBER-ISH-
Abnormal maturing T-cells	T-cell	CD3/CD2 (partial), CD7+, CD5 (partial), CD4 (partial)	TdT-, MPO-, CD34-, CXCL13-, ICOS-, PD1-,
	Myeloid	CD33 (co-expression)	MPO-, Lysozyme-
	Other	None	CD117-, CD56-, CD1a-, TCL1-
Plasmacytoid dendritic cells	Plasmacytoid DC	CD123+, CD303+, CD4+, CD7+, CD68+	TCL1-, CD56-
B-cells (mantle)	B-cell	CD20, PAX5 background follicles	

Cytogenomics

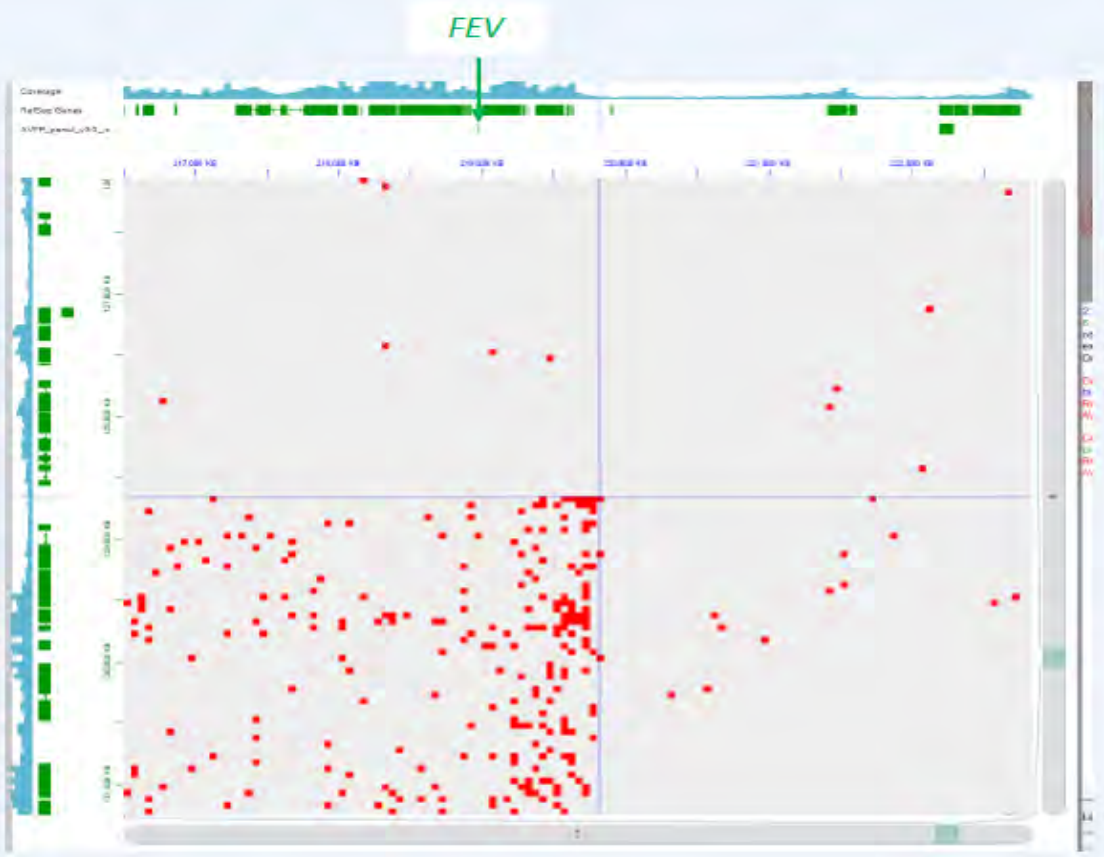
Specimen	Cells	Alterations	Details
Right Axillary Lymph Node	40–60%	**10q cnLOH** (PTEN) (69,635,024-135,424,645)x2 hmz	**~66 Mb** region (10q21.3–q26.3); encompasses PTEN (10q23.31) tumor suppressor as well as FGFR2 (10q26.13)
	40–60%	**2q Loss (partial monosomy)** (220,698,125-243,052,331)x1	**~22 Mb** region (2q35–q37.3); LRP1B (2q37.1) , PDCD1 (2q37.3; PD1), NFE2L3 (~2q37.2)
	40–60%	**6q Gain (partial trisomy)** (128,998,864-170,976,062)x3	**~42 Mb** region (6q22.33–q27) MYB (6q23), PLAG1(6q24.3), HACE1(6q24), ARID1B (6q25.3)
Bone Marrow	Normal	No alterations (Diploid)	

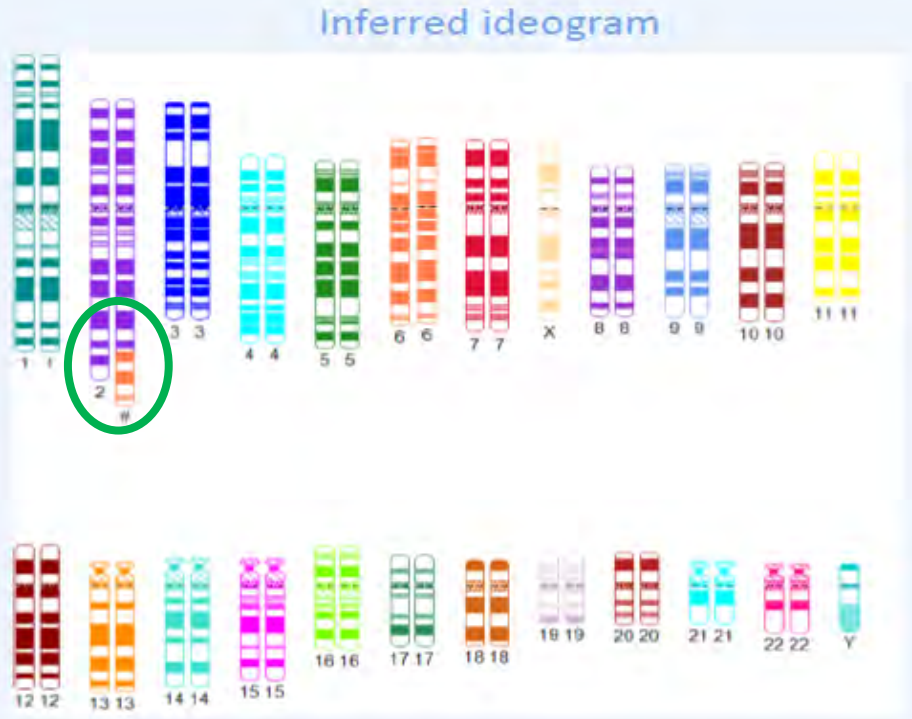
ARIMA Hi-C Assay
(High-throughput genome wide chromosome conformation capture)

Der(2) t(2;6)(q35;q22.33) in the proximity of FEV

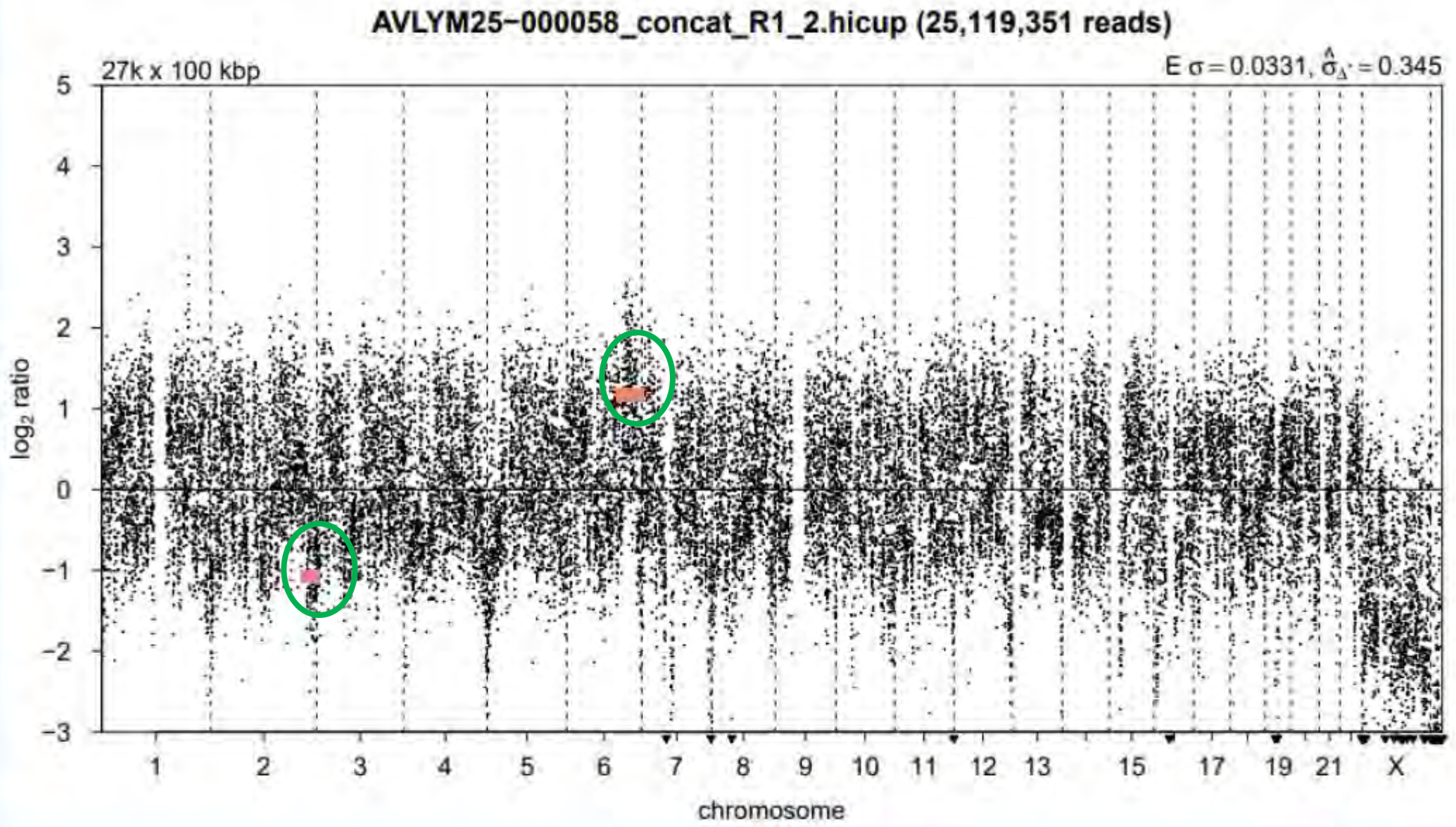
Unbalanced 2q-/6q+ translocation (breakpoint within 1.0 Mb near FEV gene)

FEV gene also known as PET1 or ETS transcription factor





46<2n>,XY,der(2)t(2;6)(q35;q22.33)



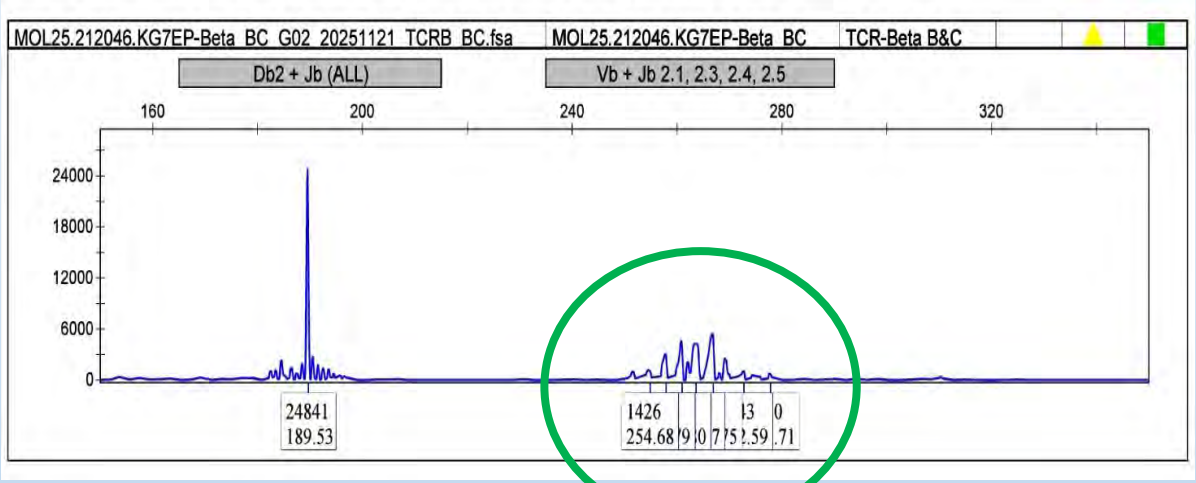
CNV (RUO): Matches microarray of 2q- and 6q+

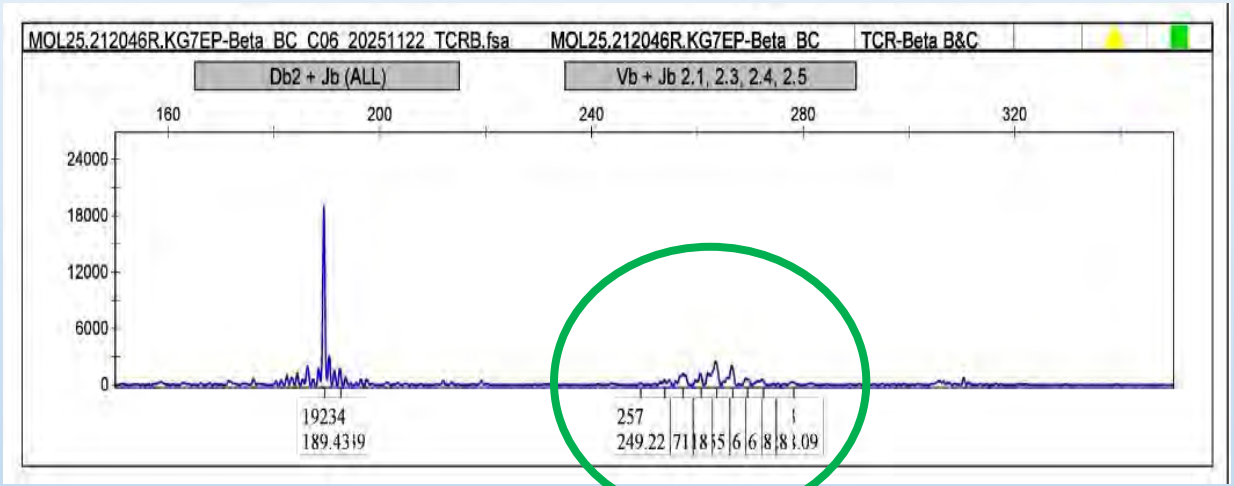
Shared variants

Gene	Protein Change	cDNA Change	Marrow VAF (%)	Axillary Node VAF (%)	Cervical Node VAF (%)	Clinical Significance
TET2	p.Asn275fs	c.822delC	**6.6**	**35.7**	**40.8**	**Tier 2 Prognostic**
TET2	p.Gly1370Glu	c.4109G>A	**5.8**	**31.8**	**41.7**	**Tier 2 Prognostic**
DNMT3A	p.Gly413fs	c.1238delG	**<5**	**32.1**	**39.5**	**Tier 2**
DNMT3A	splice_donor	c.1667+1_1667+2insA	**30.6**	**33.6**	**42.1**	**Tier 2**
CEBPA	p.Gly242Ser	c.724G>A	**55.4**	**54.5**	**58.4**	Germline/CH (~50-60%); VUS (C-terminal bZIP; non-polar to polar)
SOCS1	p.Arg20Leu	c.59G>T	**46.6**	**53.4**	**48.6**	Germline-like JAK/STAT

Right axillary LN : TCR beta gene rearrangement

Panel	V/J Region	Size (bp)	Run 1	Run 2
Beta BC	Vβ2.x/Jβ	189.5	24,841	19,234
Beta BC	Db2/Jβ ALL	254.7	7,752	711





Why "Borderline Positive"?

Limited V Usage (Incomplete DJ-Dominant):

- ✗ **No complementary Vβ-Jβ panel** showing mature VDJ rearrangement
- ✗ **DJ-only = 13 Jβ combinations** (vs 52 Vβ for diversity)
- ✗ Polyclonal mimicry possible (reactive oligoclonal expansion)
- ✓ **Reproducible across runs** (true clone vs artifact)
- ✓ **High peak height** (20k+ fluorescence units)

Diagnostic Confidence Hierarchy

Level 1 (Definite Polyclonal)

VDJ polyclonal = 95% NPV for lymphoma

Level 2 (Likely Monoclonal)

VDJ clonal = 85-90% PPV for lymphoma

Level 3 – this case

DJ-only clonal = 60% PPV for lymphoma ← Borderline

Level 4 (Definite Clonal)

VDJ + TCRγ concordant clonal = >95% PPV

Site-specific unique variants

Gene	Protein Change	cDNA Change	Marrow VAF (%)	Axillary Node VAF (%)	Cervical Node VAF (%)	Site Distribution	Clinical Significance
DNMT3A	p.Phe751Leu	c.2253C>G	9.3	Absent	Absent	Marrow-only	Tier 2 missense p.F751L
NRAS	p.Gly13Arg	c.37G>C	Absent	9.3	Absent	Axillary-only	Tier 2
KRAS	p.Gly13_Val14insGly	c.38_40dupGCG	Absent	Absent	36.7	Cervical-only	Not curated; but it is in the hotspot domain
PTEN	p.Glu242_Phe243insGlyGlyGlu (Exon 7, near F241S hotspot)	c.726_727insGGTGGCGAG	Absent (6.0 trace)	Absent	80.8	Cervical-only	VUS (likely C2 domain insertion (near F241S hotspot) likely pathogenic LoF → PI3K/AKT hyperactivation
SETBP1	p.His1158Arg	c.3473A>G	Absent	Absent	5.1	Cervical-only	VUS

Differentials

- PTCL – NOS
- T-ALL/LBL
- ETP-ALL
- BPDCN
- Myeloid/Lymphoid Neoplasms with eosinophilia and tyrosine kinase gene fusions
- AML with aberrant T-cell markers/ALAL/MPAL

PTCL-NOS

- ✓ Multi-station lymphadenopathy
- ✓ Morphology+ Flow and IHC: CD4+ with partial loss of pan-T(flow)
- ✓ GATA3 and mature pDC (TFH-lymphoma)
- ✓ Co-occurrence of Multiple TET2 and DNMT3A mutations (×2)
- (TBX21 group)
- ✓Arm-level CNAs with PTEN cnLOH
- (GATA3-like subgroup)
- ✓ T-cell receptor beta gene rearrangement

- ✗ **Lack of follicular expansion/TFH phenotype**
- ✗ **CD34, MPO positive T-cells**
- ✗ **No complementary Vβ-Jβ panel** showing mature VDJ rearrangement
- ✗ **DJ-only = 13 Jβ combinations** (vs 52 Vβ for diversity)

ETP-ALL

- ✓ CD34✓ **Multi-station lymphadenopathy**
- ✓ **Morphology**
- , TdT-CD7 coexpression
- ✓ Partial T-antigen loss (by IHC)
- ✓ Upregulation of myeloid genes (MPO)
- ✓ DJ-dominant TCRB
- ✗ **Age > 65**
- ✗ **Absence of mediastinal mass**
- ✗ **Lack of high circulating blasts**
- ✗ TET2/DNMT3A mutations (rare)
- ✗ Arm-level CNAs with PTEN cnLOH

Blasts: cCD3+, CD1a-, CD8-, absent or dim CD5 expression (< 75% positive blasts) and expression of one or more myeloid (CD11b, CD13, CD33, CD65, KIT [CD117]) and/or stem cell (CD34, HLA-DR) markers (≥ 25% positive blasts), and negative myeloperoxidase (< 3%).

MPO is positive

T-ALL/LBL

Polycomb (EZH2, SUZ12)
NOTCH1/FBXW7/IL7R/JAK3/
STAT5B mutations

Usually lower genomic complexity-
CDKN2A/2B deletion,
TCR translocations -TAL1/TLX/HOXA
rearrangements,

BPDCN

- ✓ Multi-station lymphadenopathy
- ✓ Morphology+ Flow and IHC: CD4+ with partial loss of pan-T(flow)
- ✓ CD123 and CD303 positive
- ✓ TET2 mutations (×2)
- ✓ NRAS mutations
- ✗ **Lack of existing or prior myeloid neoplasms**
- ✗ PTCL + BPDCN – Not reported
- ✗ Negative CD56 and TCL1
- ✗ **DNMT3A mutations**
- ✗ **Arm-level CNAs with PTEN cnLOH**
- ✗ **CD34, MPO positive T-cells**
- ✗ **No complementary Vβ-Jβ panel** showing mature VDJ rearrangement
- ✗ **DJ-only = 13 Jβ combinations** (vs 52 Vβ for diversity)

DNMT3A rare

PTEN loss via cnLOH at 10q is not reported as a recurrent event

DNMT3A rare or uncommon

BPDCN shows a distinctive genomic landscape compared to AML and related neoplasms, with a predominance of mutations in **TET2, ASXL1, NRAS**, and splicing factor genes (SRSF2, ZRSR2)

BPDCN frequently shows widespread CNAs, but they are usually focal

MPAL T/myeloid

- ✓ Blasts: myeloid/T markers
- ✓ Bialleilic TET2 mutations
- ✓ Bialleilic DNMT3A mutations (×2)
- ✓ Germline CEBPA mutations (VUS)
- ✓ DJ-dominant TCRB (immature pre-thymic)
- ✗ Multi-level lymphadenopathy
- ✗ Flow: Lack of distinct blasts
- ✗ Lack of bone marrow or peripheral blood involvement

AML with aberrant T-cell markers

Final Diagnosis

De Novo T/myeloid MPAL ,

Presenting as Isolated Extramedullary (LN-based) Non-Leukemic Myeloid sarcoma in a background of maturing abnormal T-cells (mimicking PTCL)

WHO-HAEM5 2022

Acute leukemia of ambiguous lineage with defining genetic abnormalities

- Mixed-phenotype acute leukaemia with BCR::ABL1 fusion
- Mixed-phenotype acute leukaemia with KMT2A rearrangement
- Mixed-phenotype acute leukemia with ZNF384 rearrangement (B/
- Acute leukaemia of ambiguous lineage with BCL11B rearrangement

Acute leukemia of ambiguous lineage defined immunophenotypically

- Mixed-phenotype acute leukemia, B/myeloid
- Mixed-phenotype acute leukemia, T/myeloid
- Mixed-phenotype acute leukemia, rare types
- Acute leukemia of ambiguous lineage NOS
- Acute undifferentiated leukemia

T/Myeloid MPAL: Known Genomic Context

- **Recurrent Drivers (~30-50%):** (KMT2A-r (t(v;11q23), 20-40% pediatric B/M), Ph+ t(9;22) BCR::ABL1 (15-30% adults), ZNF384-r (40% pediatric B/M).

- MPAL-T/M: BCL11B, Biallelic WT1 alterations, FLT3 alterations, PHF6 mutation, RUNX1 mutation, PICALM::MLLT10 rearrangement

- **Epigenetic dominance:**

Epigenetic (DNMT3A 20-33%, TET2/IDH2/EZH2/ASXL1), signaling (FLT3/NRAS/KRAS 10-20%), TFs (RUNX1/WT1/CEBPA 10-20%), T-ALL (NOTCH1/FBXW7/IL7R/JAK3/PHF6 ~10-20% T/M

- **RAS/STAT pathway:**

10–40% of cases; patient has NRAS, KRAS, with PTEN loss (tumor suppressor inactivation)

- **Absent typical T-ALL drivers:**

No NOTCH1/FBXW7 (>75% T-ALL), EZH2, PHF6—argues against pure T-ALL diagnosis

MPAL cases (n=176) were categorized into eight distinct Subgroups (G1–G8)

Stem-cell disease-like and common myeloid progenitor disease-like signatures

G1 was associated with CEBPA mutations,
G2 and G3 with NOTCH1 mutations,
G4 with BCL11B rearrangement and FLT3 mutations,

Granulocyte-monocyte progenitor/monocyte disease-like signatures:
G5 with BCR::ABL1 fusion
G6 with KMT2A rearrangement/KMT2A rearrangement-like features

Common-lymphoid progenitor disease-like signatures:
G7 with ZNF384 rearrangement/ZNF384 rearrangement-like characteristics.
G8 with BCR::ABL1 fusion

> Am J Hematol. 2023 Jan;98(1):66-78. doi: 10.1002/ajh.26758. Epub 2022 Oct 31.

Integrative genomic and transcriptomic profiling reveals distinct molecular subsets in adult mixed phenotype acute leukemia

Qian Wang [1,2], Wen-Zhi Cai [1,2], Qin-Rong Wang [1,2], Ming-Qing Zhu [1,2], Ling-Zhi Yan [1,2], Yan Yu [1,2], Xie-Bing Bao [1,2], Hong-Jie Shen [1,2], Hong Yao [1,2], Jun-Dan Xie [1,2], Tong-Tong Zhang [1,2], Ling Zhang [1,2], Xiao-Yu Xu [1,2], Zhe Shan [1,2], Hong Liu [1,2], Jian-Nong Cen [1,2], Dan-Dan Liu [1,2], Jin-Lan Pan [1,2], Da-Ru Lu [3,4], Jia Chen [1,2], Yang Xu [1,2], Ri Zhang [1], Ying Wang [1,2], Sheng-Li Xue [1,2], Miao Miao [1,2], Yue Han [1,2], Xiao-Wen Tang [1,2], Hui-Ying Qiu [1,2], Ai-Ning Sun [1,2], Jin-Yan Huang [5,6], Hai-Ping Dai [1,2], De-Pei Wu [1,2], Su-Ning Chen [1,2]

Affiliations — collapse

Affiliations

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2 Institute of Blood and Marrow Transplantation, Collaborative Innovation Center of Hematology, Soochow University, Suzhou, People's Republic of China.
3 Key Laboratory of Birth Defects and Reproductive Health of National Health Commission, Chongqing Population and Family Planning, Science and Technology Research Institute, Chongqing, People's Republic of China.

T/Myeloid MPAL-NOS

More mutations in NOTCH1, JAK3, and transcriptional regulation genes, including CEBPA, GATA2, PHF6, and WT1.

MYELOID NEOPLASIA | MAY 1, 2025

Defining 2 biologically and clinically distinct groups in acute leukemia with a mixed phenotype

Pallavi Galera, Deepika Dilip, Andriy Derkach, Alexander Chan, Yanming Zhang, Sonali Persaud, Tanmay Mishra, Kyle Kramer, Mahak Kathpalia, Ying Liu, Christopher Famulare, Qi Gao, Douglas A. Mata, Maria Arcila, Mark B. Geyer, Eytan Stein, Ahmet Dogan, Mikhail Roshal, Ross L. Levine, Jacob Glass, Wenbin Xiao

Blood (2025) 145 (18): 2056–2069.

https://doi.org/10.1182/blood.2024026273

Article history

Connected Content

A commentary has been published: Mixed-phenotype acute leukemia revisited: omics lead the way

Key Points

- AML-MP and MPAL are biologically distinct despite sharing features of MP.
- AML-MP and MPAL have differential responses to therapies.

› Blood. 2007 Nov 15;110(10):3706-14. doi: 10.1182/blood-2007-02-073486. Epub 2007 Aug 1.

Distinct gene expression profiles of acute myeloid/T-lymphoid leukemia with silenced CEBPA and mutations in NOTCH1

Bas J Wouters [1], Meritxell Alberich Jordà, Karen Keeshan, Irene Louwers, Claudia A J Erpelinck-Verschueren, Dennis Tielemans, Anton W Langerak, Yiping He, Yumi Yashiro-Ohtani, Pu Zhang, Christopher J Hetherington, Roel G W Verhaak, Peter J M Valk, Bob Löwenberg, Daniel G Tenen, Warren S Pear, Ruud Delwel

Affiliations – collapse

Affiliation

1 Department of Hematology, Erasmus University Medical Center, Rotterdam, The Netherlands.

PMID: 17671232 PMCID: PMC2077318 DOI: 10.1182/blood-2007-02-073486

#	Author(s)	Year	Site of MPAL Sarcoma / Extramedullary Disease	Type (B/Myeloid vs T/Myeloid)	Prior Diagnosis / Context
1	Hossain D et al.	1999	Cervical lymph node	T/Myeloid (mixed myeloid/T-cell)	CML progressing to blast crisis (not de novo)
2	Vega et al.	2008	Pleura	B/Myeloid (biphenotypic leukemia)	Relapse after allogeneic stem cell transplantation for biphenotypic leukemia
3	Alrumaih R et al.	2013	Lateral pharyngeal wall	B/Myeloid (acute biphenotypic leukemia)	31 yo; Relapse after autologous stem cell transplantation
4	Khanna G et al.	2017	Thyroid gland	B/Myeloid (mixed myeloid/B-cell)	58 years; Underlying MPAL (marrow involvement present)
5	Takakuwa T et al.	2018	Pleura and lymph nodes	B/Myeloid, NOS	Without concurrent/antecedent blood or bone marrow involvement)
6	Wang C et al.	2018	Intestinal (epitheliotropic sarcoma)	T/Myelomonocytic with t(9;22) BCR-ABL1	Without concurrent/antecedent blood or bone marrow involvement
7	Means J et al.	2022	Anterior mediastinum, pericardium, pleura	B/Myeloid	De novo (no marrow or peripheral blood leukemia)
8	Santiago-Negron CL et al.	2025	Occipital Lymph node	T/Myeloid with BCR::ABL1	Occipital LN; Concurrent bone marrow involvement
9	Zhou Y et al.	2025	Not specified (atypical presentation)	MPAL with atypical BCR::ABL1 e13a3 fusion	Concurrent marrow involvement

ORIGINAL ARTICLES

t(8;13)-positive Bilineal Lymphomas

Report of 6 Cases

Vega, Francisco MD, PhD; Medeiros, L. Jeffrey MD; Davuluri, Rajayogesh; Cromwell, Candy C. BS; Alkan, Serhan MD
Abruzzo, Lynne V. MD, PhD

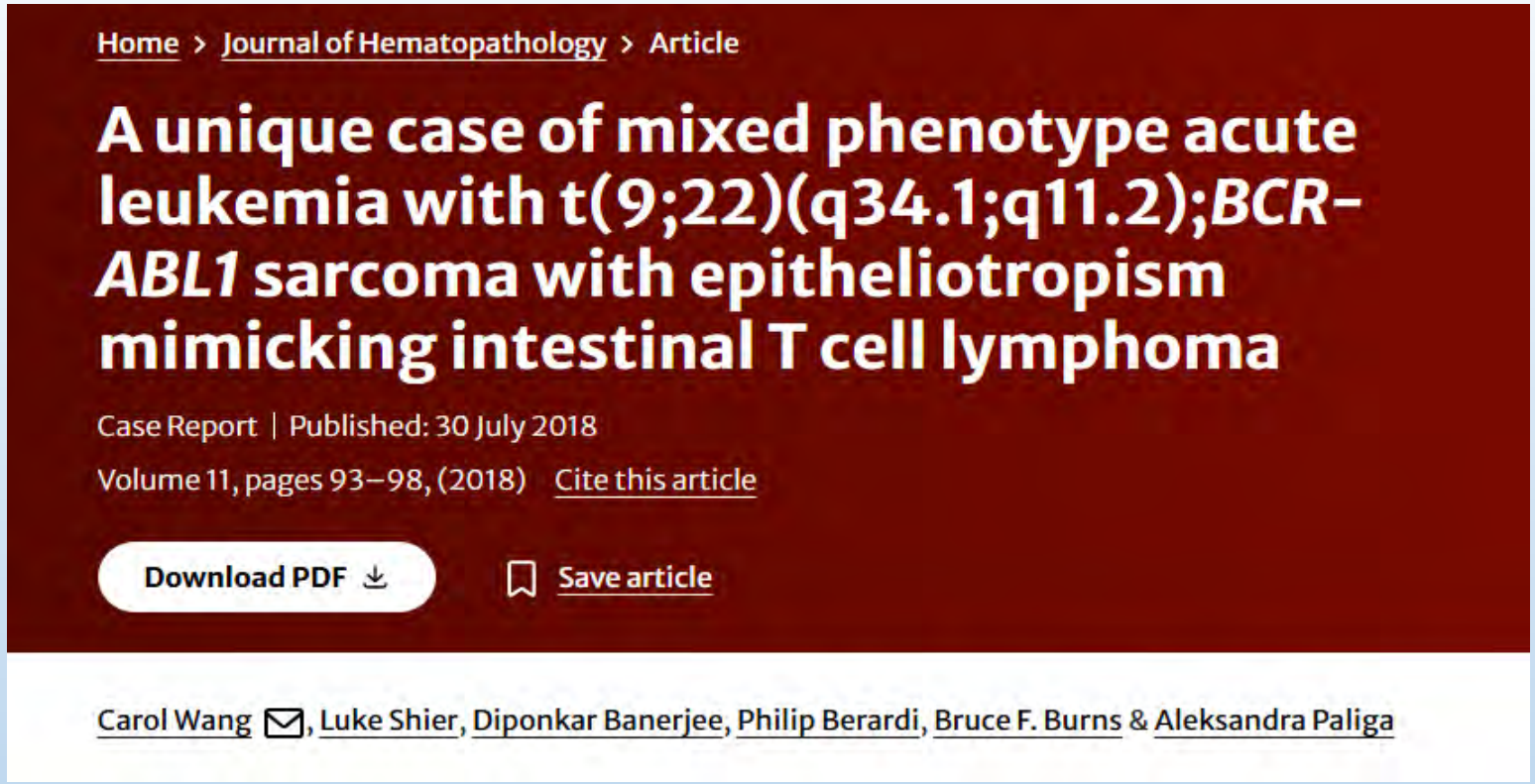
Author Information

The American Journal of Surgical Pathology 32(1):p 14-20, January 2008. | **DOI:** 10.1097/PAS.0b013e31814b226e

Abstract

Now termed as "Myeloid/lymphoid neoplasm with FGFR1 rearrangement"

The 8p11 myeloproliferative syndrome (EMS) is a rare hematologic malignancy characterized by myeloid hyperplasia, eosinophilia, and precursor lymphoblastic lymphoma, associated with balanced translocations involving chromosome 8p11, most commonly t(8;13)(p11;q12). Approximately 75% of EMS patients present with or develop precursor T-cell lymphoblastic lymphoma, and most subsequently develop acute myeloid leukemia. Here we describe the morphologic and immunophenotypic features of 6 cases of t(8;13)-positive bilineal lymphoma of mixed T-cell and myeloid lineage, 5 in lymph nodes and 1 in breast. The patients, 3 males and 3 females, ranged in age from 6 to 19 years. Histologically, each tumor was composed of 2 distinct



Home › Journal of Hematopathology › Article

A unique case of mixed phenotype acute leukemia with t(9;22)(q34.1;q11.2);*BCR-ABL1* sarcoma with epitheliotropism mimicking intestinal T cell lymphoma

Case Report | Published: 30 July 2018

Volume 11, pages 93–98, (2018) Cite this article

Download PDF Save article

Carol Wang, Luke Shier, Diponkar Banerjee, Philip Berardi, Bruce F. Burns & Aleksandra Paliga

In addition to CD4 and CD7 expression, the atypical cells were also positive for CD34 (subset), CD68, muramidase/lysozyme, and CD117

Myelomonocytic differentiation was confirmed based on blast expression of CD11c and CD64, with concurrent CD11c, dim CD13, bright CD33, dim CD71, partial CD117, and partial CD34 positivity. The blast population was myeloperoxidase negative (ETP-ALL ??).

blood

ISSUES FIRST EDITION ABSTRACTS COLLECTIONS AUT

MYELOID NEOPLASIA | MAY 1, 2025

Mixed-phenotype acute leukemia revisited: omics lead the way

Lars Bullinger

Blood (2025) 145 (18): 1969–1971.

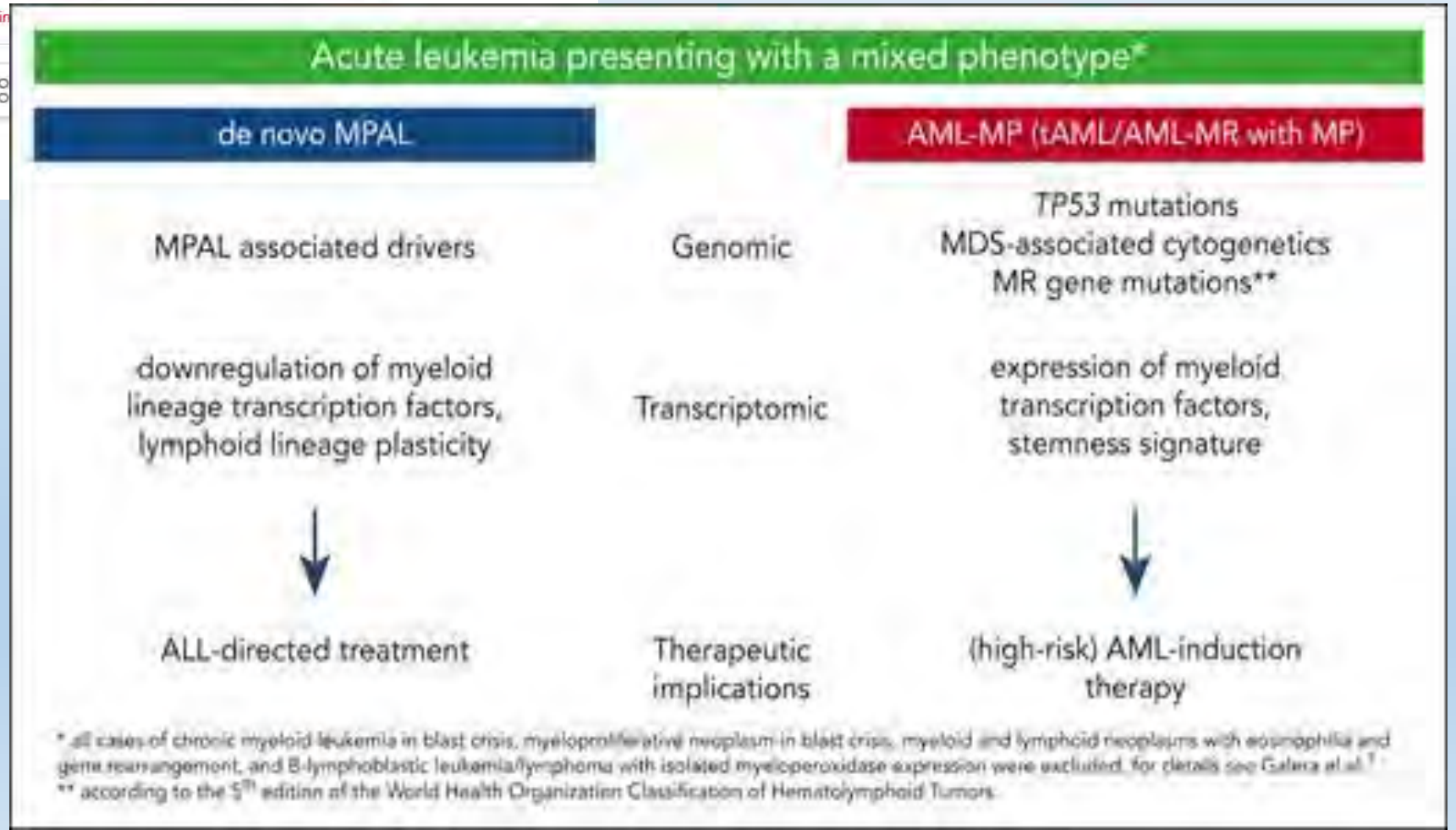
https://doi.org/10.1182/blood.2025028351

Connected Content

This is a commentary to: Defining 2 biologically and clinically distin

Split-Screen

Subjects: Free Research Articles



Follow up : Sequential therapy rationale

Initial CHOP (T-cell directed) → partial response, then progression

Duvelisib (PI3K inhibitor; 75mg BD for one month) → clinical LAD reduction

Mini-CVD + venetoclax → T-ALL-like regimen targeting epigenetic mutations (TET2/DNMT3A) preferred for epigenetic-dysregulated MPAL

Response

- Partial metabolic response (PET SUVmax ↓ from 5.2 → 4.4)
- Reduced LAD (cervical resolution, residual inguinal <1 cm)
- Platelet count improved – 90k/cmm

Ongoing

- Allo-SCT consideration

Summary

- Rare presentation of extramedullary-only T/myeloid MPAL
- Higher expression of myeloid markers - TdT+/sCD3 weak subset + MPO/lysozyme/CD33/CD117/CD34 subsets
- limited TCRβ usage (Dβ-Jβ only, immature)
- Significant overlap in genomic profile with PTCL-NOS, BPDCN
- Correlates with G1 cluster described by Wang et al. 2022 (Biphenotypic, Higher myeloid expression, Germline Tier 3 CEBPA variant) background

Summary

- Notably, duvelisib responsiveness harnessed PI3K/mTOR hyperactivation (PTEN loss synergizing TET2/DNMT3A hypermethylation, shared across PTCL/BPDCN), while CH substrate and AML-like/ETP-overlap genomics (lacking classic MPAL focal deletions IKZF1/ETV6/RB1) highlight genotype-tailored therapeutic convergence bridging diagnostic boundaries.

- Epigenetic mutations (TET2/DNMT3A) guide transition to T-ALL-like + venetoclax-based regimens

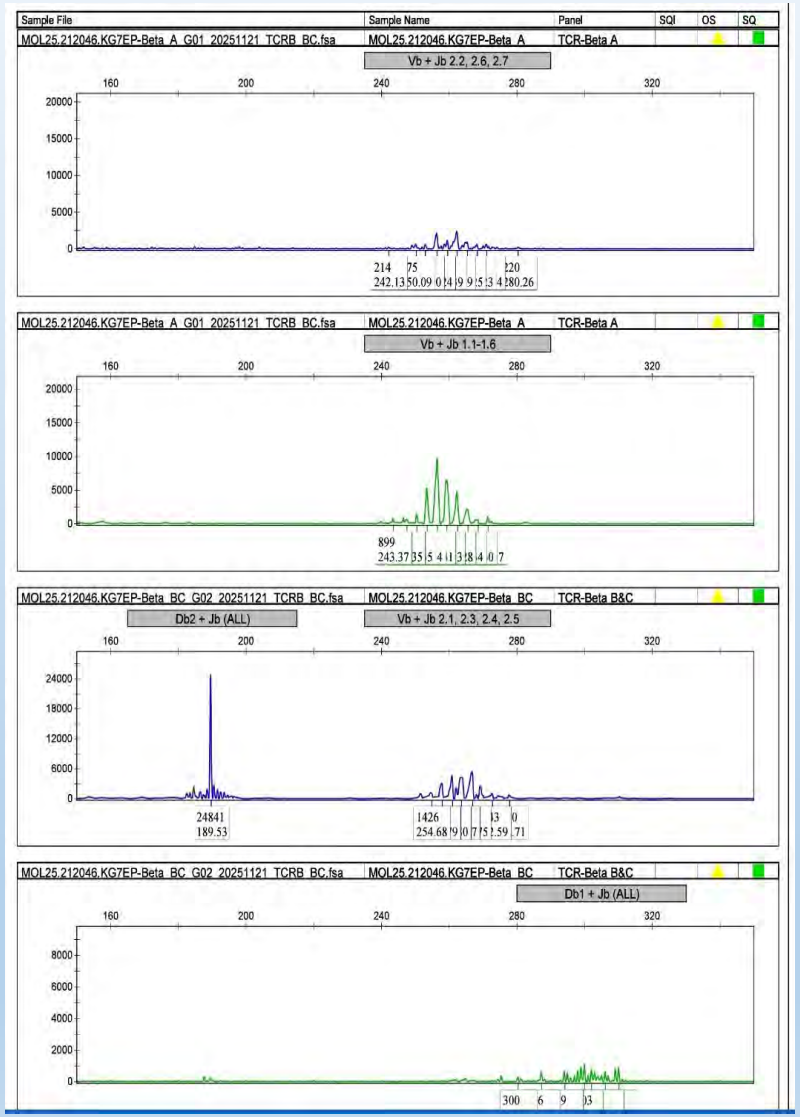
Take Away

- Comprehensive work up including extensive IHC/flow + NGS/CMA essential for accurate lineage assignment and classification of MPAL.

- Integration of CD34/TdT in the IHC panel in the lymphoma work up should be considered

Thank you

Right axillary LN : TCR beta gene rearrangement



Normal T-Cell Development (Thymus):

Pre-thymic: Dβ-Jβ rearrangement **(incomplete DJ)**

↓ Selection/maturation Post-thymic: Vβ-DJβ rearrangement **(complete VDJ)**

Critical Distinction: VDJ vs DJ-Only

Feature	Clonal VDJ	DJ-Only Clone
Diversity	**52 V segments**	**2 D segments only**
FP Rate	**<5%**	**15-25%**
Maturity	**Post-thymic (mature)**	Pre/pro-thymic (immature)
Lymphoma PPV	**85-90%**	<60%

BIOMED-2 PCR Strategy

TCR-Beta A Panel

- Vβ 1.1-1.6 consensus primers
- Jβ consensus primers
- Detects: **Complete VDJ**
- Mature rearrangements

TCR-Beta BC Panel

- Vβ 2.1-2.7 consensus primers
- Db1/Db2-Jβ primers
- Detects: **Incomplete DJ**
- Immature rearrangements

Cytogenomics

ARIMA Hi-C: Unbalanced 2q-/6q+ translocation (breakpoint within 1.0 Mb near FEV)

2q loss and 6q gain CNAs arise from a single structural event rather than independent segmental alterations detected by CMA.

Genome-wide chromosome conformation capture assay

Map physical contacts between chromatin regions via “Off-diagonal” interaction pattern

A unique case of mixed phenotype acute leukemia with t(9;22)(q34.1;q11.2);*BCR-ABL1* sarcoma with epitheliotropism mimicking intestinal T cell lymphoma

Case Report | Published: 30 July 2018

Volume 11, pages 93–98, (2018) Cite this article

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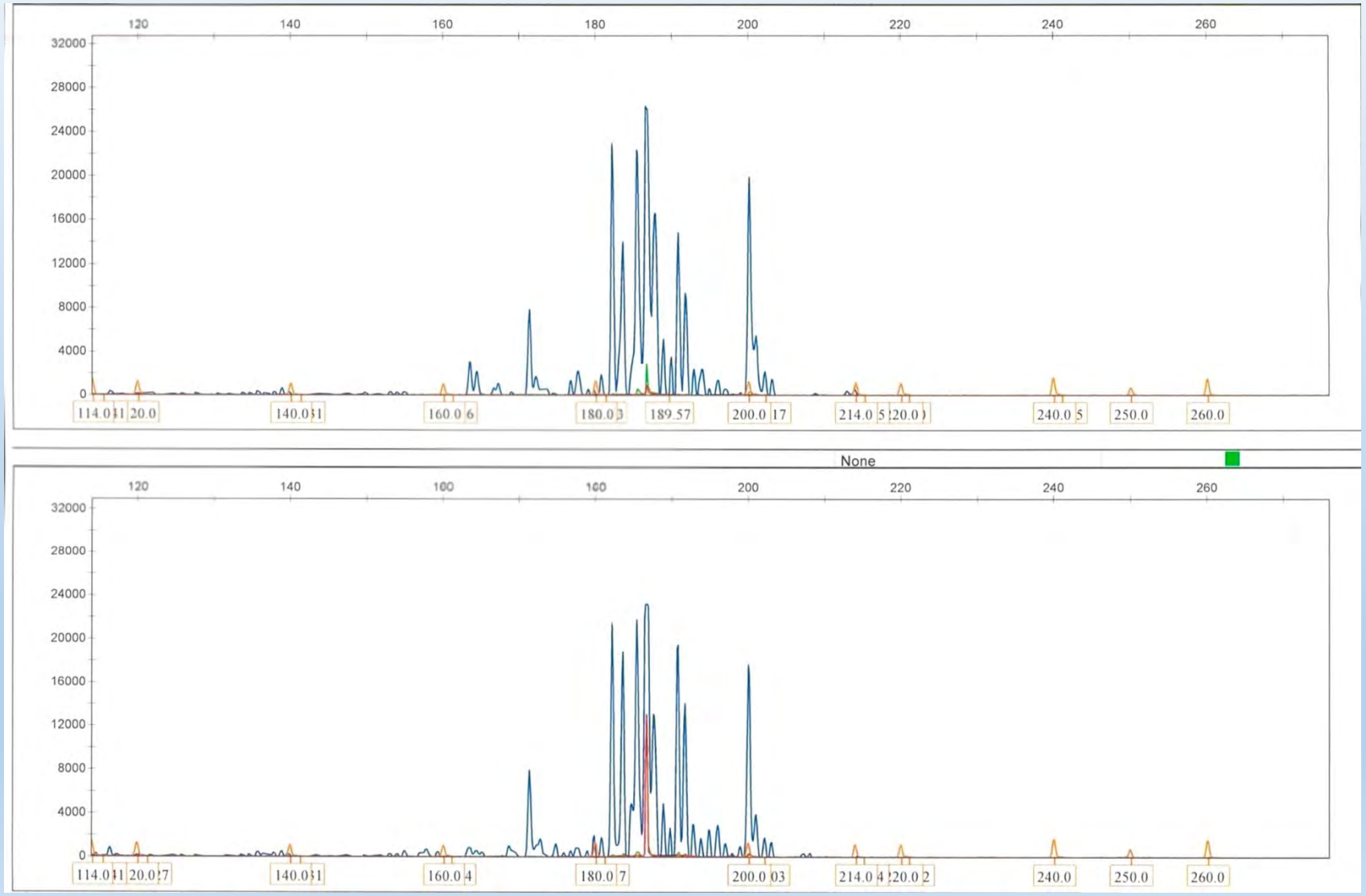
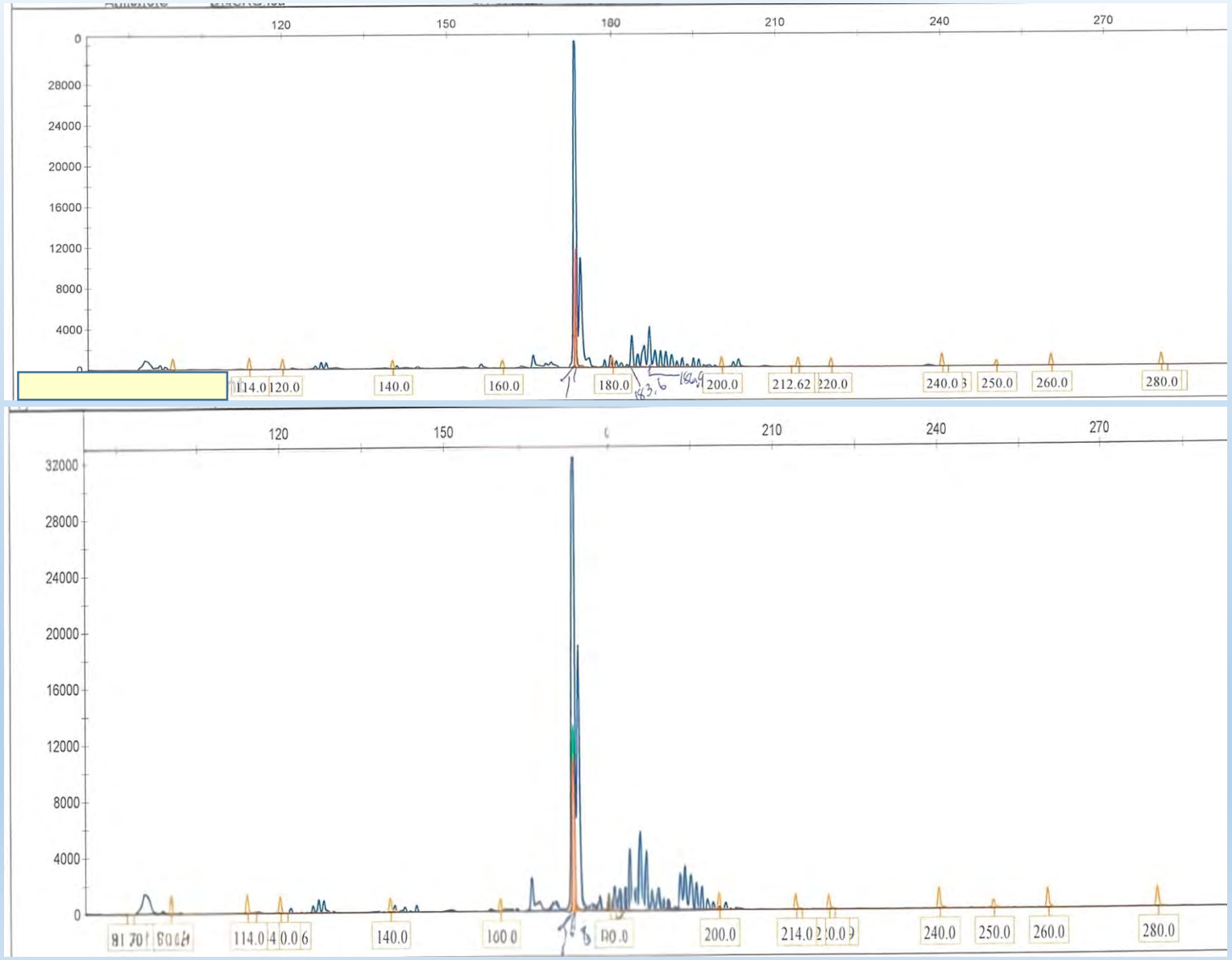
Carol Wang, Luke Shier, Diponkar Banerjee, Philip Berardi, Bruce F. Burns & Aleksandra Paliga

Bone marrow: TCR gamma gene rearrangement



Oligoclonal

Left cervical LN: TCR gamma gene rearrangement



Clonal