

5TH
**World Congress of
Cutaneous Lymphomas**



Enhancing the Ability to Diagnose, Interpret and Apply Best Treatment Options for Cutaneous Lymphomas

CHALLENGING CASES IN CUTANEOUS LYMPHOMA

Bcl6 Expression in a T-cell infiltrate...

Think Follicular Helper T-cell Lymphoma

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Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Clinical history

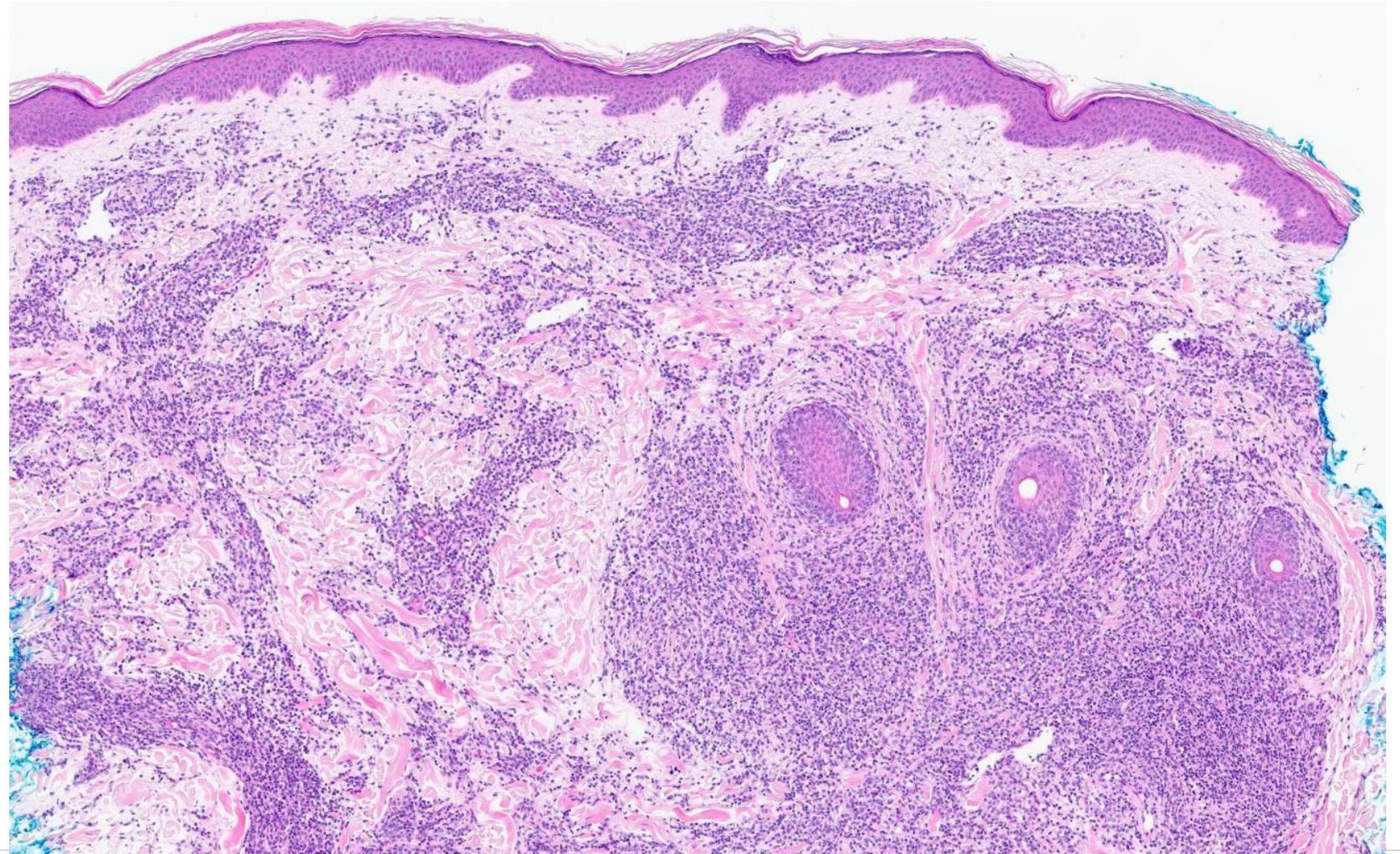
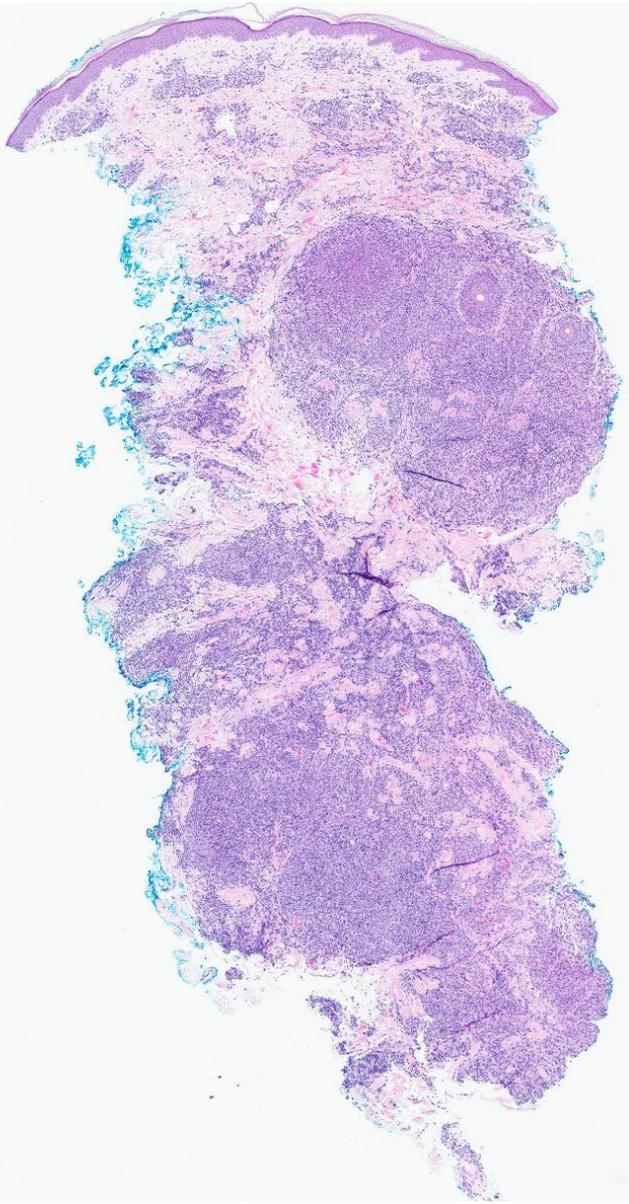
- 74 year of woman

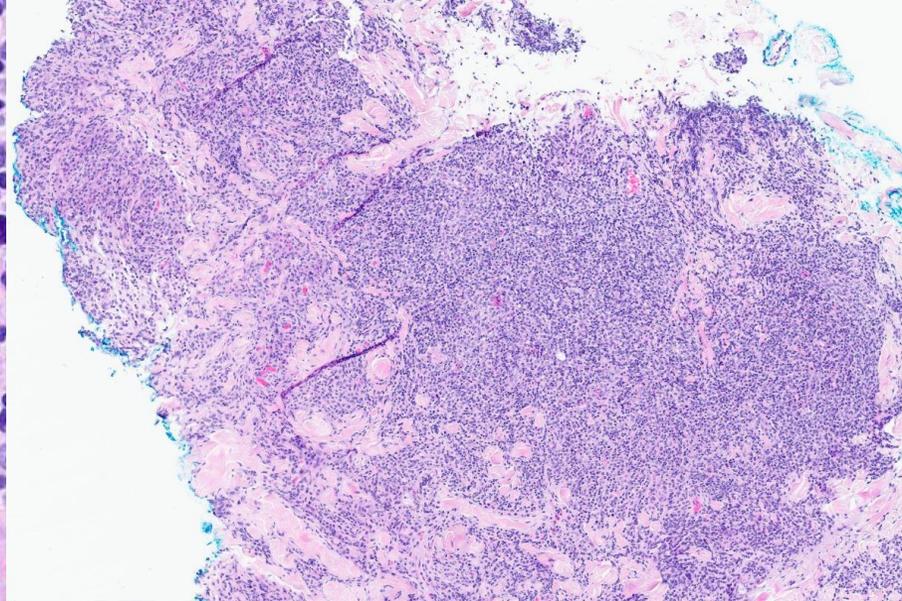
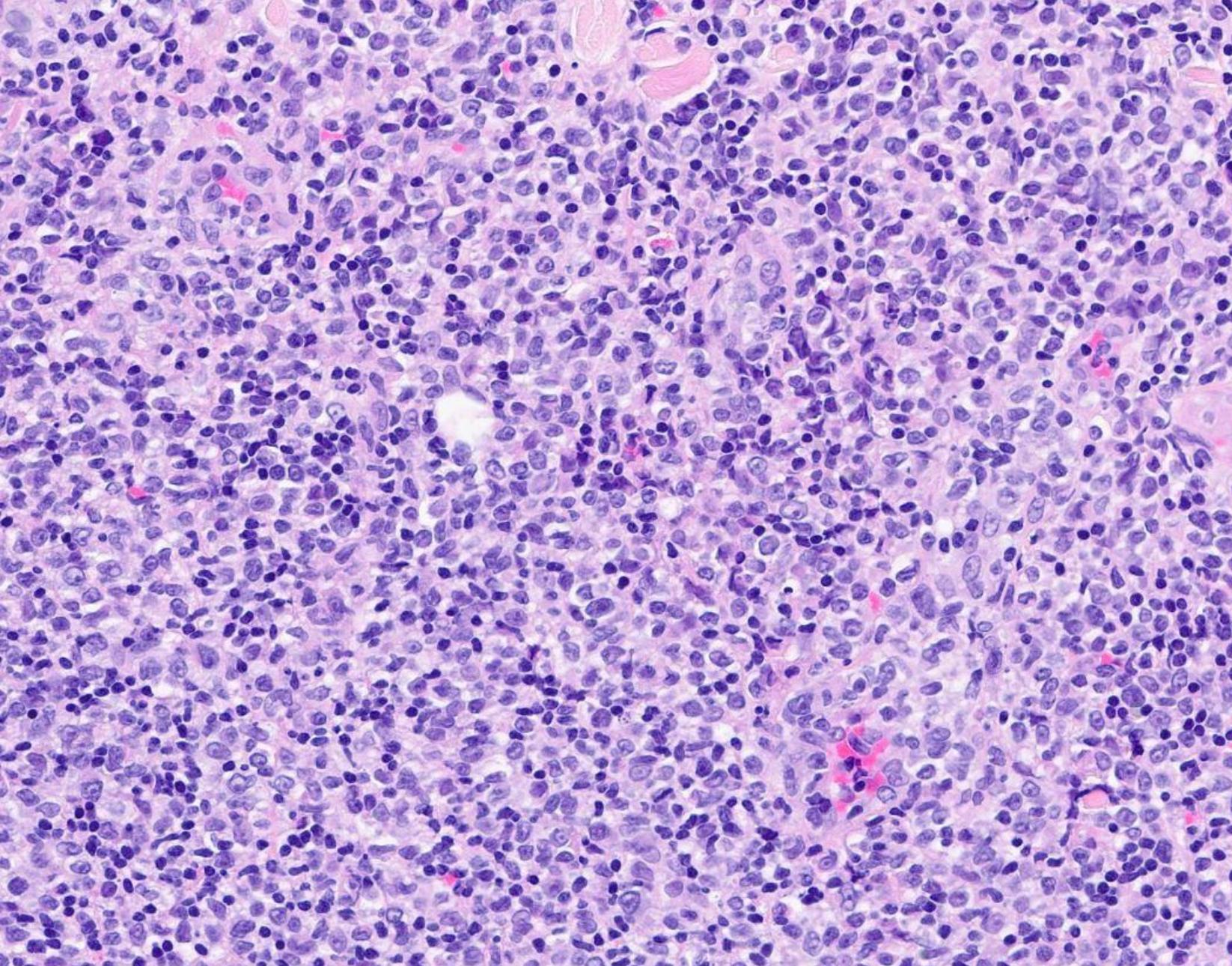
Firm pink nodule x 3 weeks: R posterior thigh

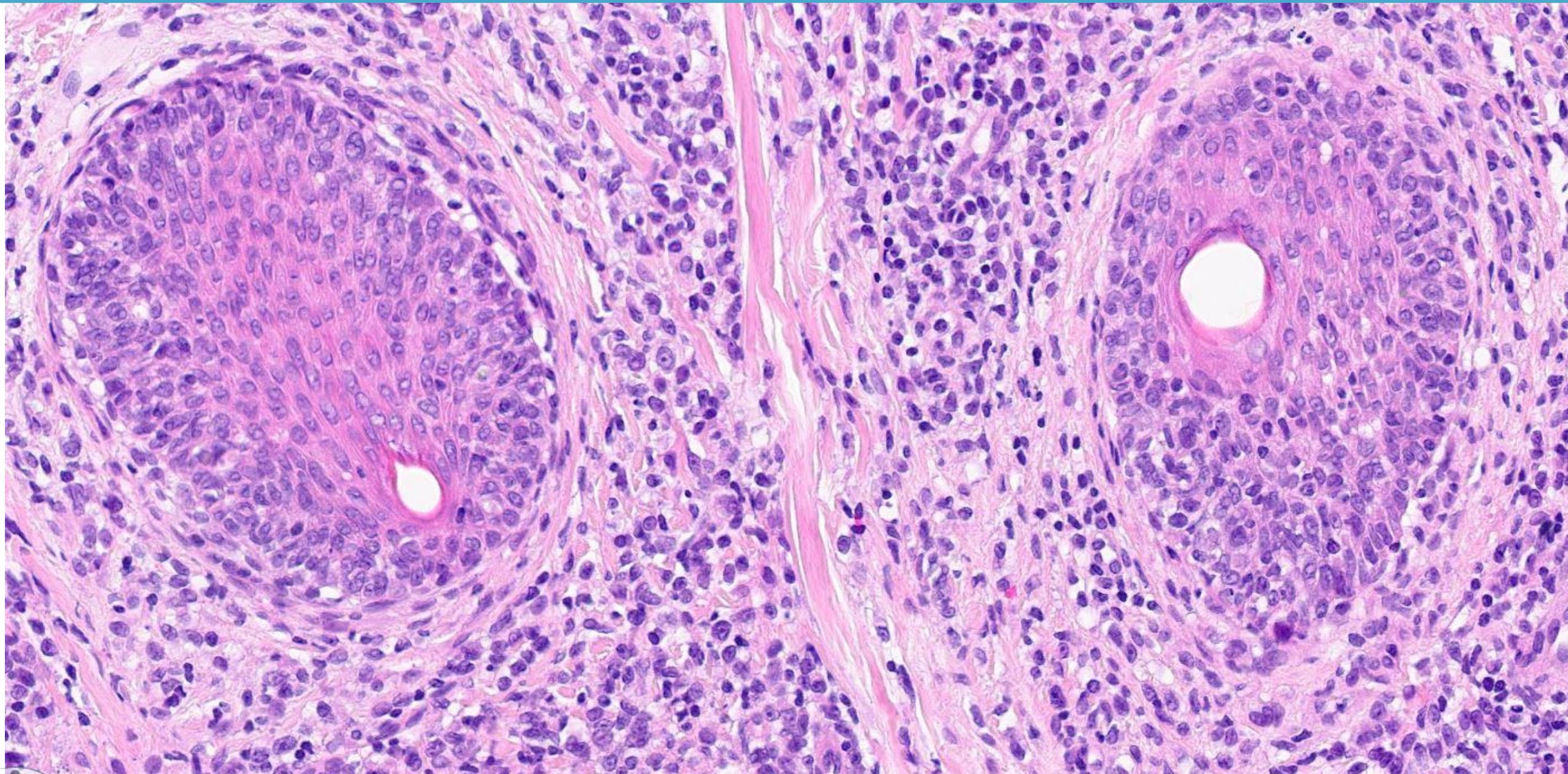
- Dx: Inflamed cyst vs furuncle vs other
- PMH: unremarkable
- Punch biopsy

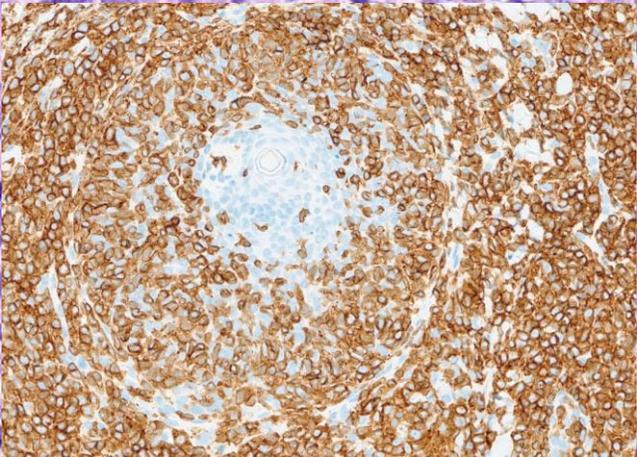
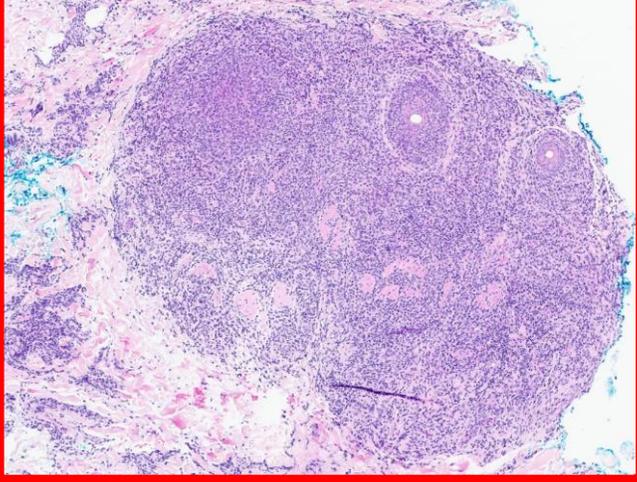
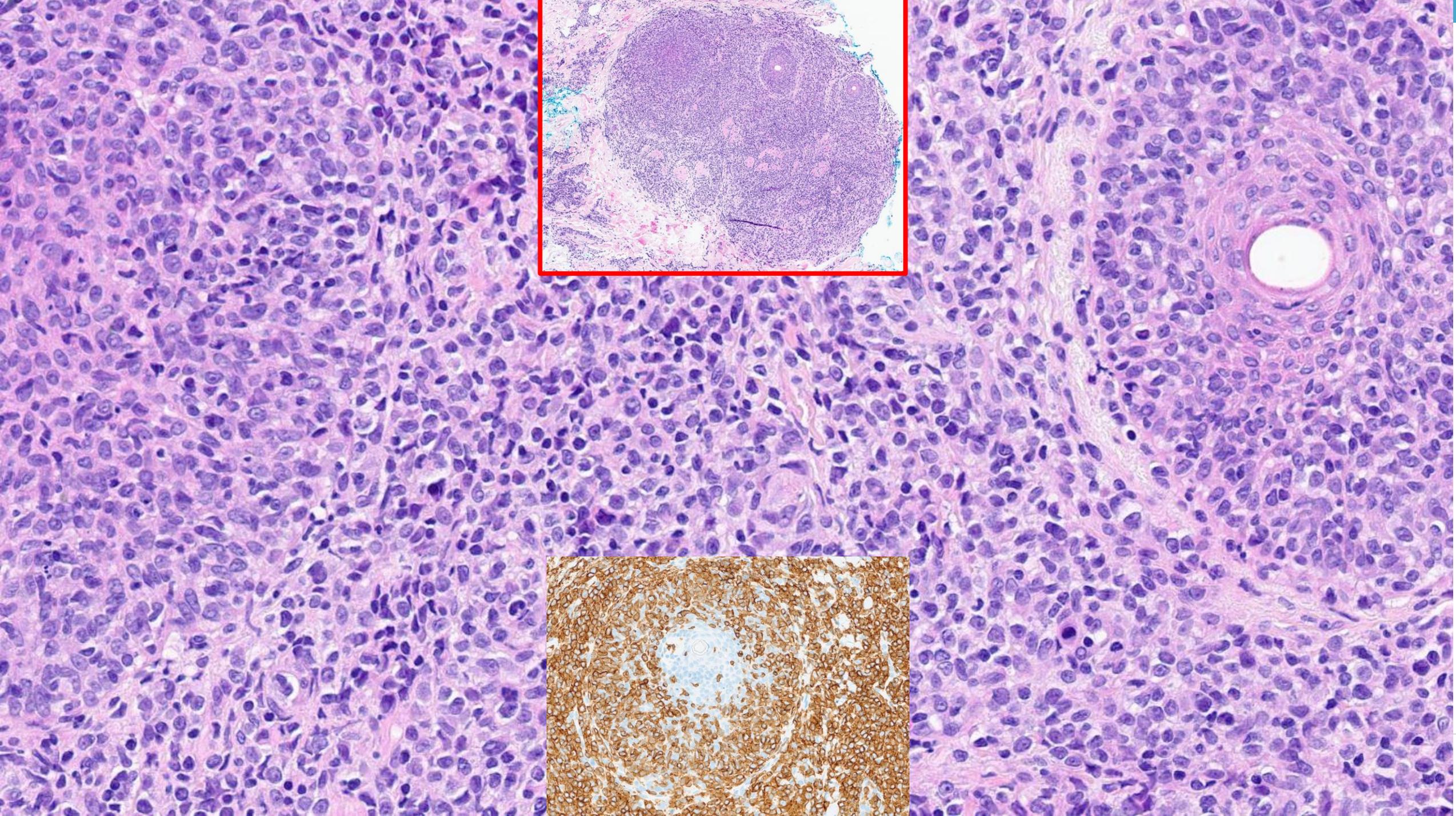


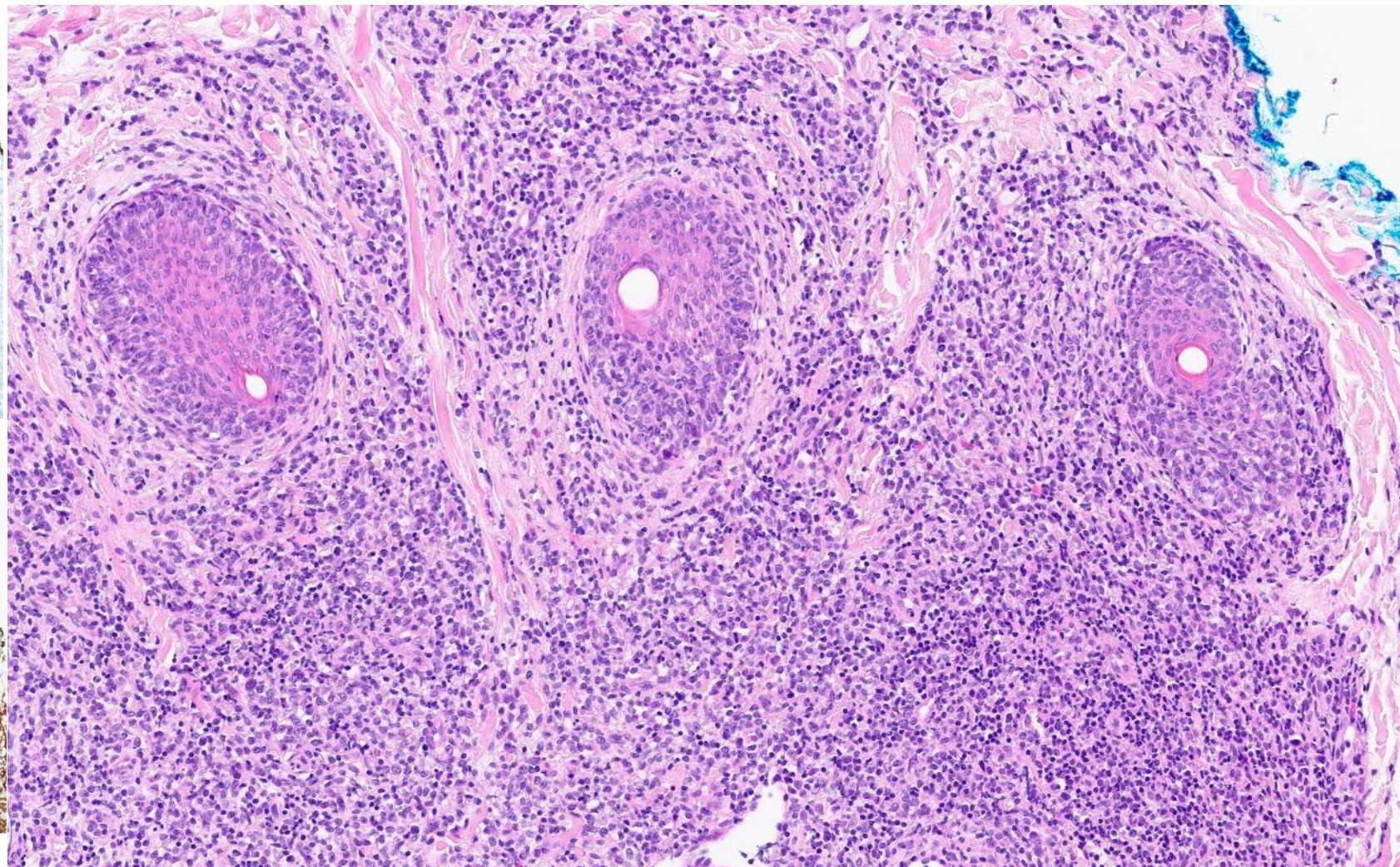
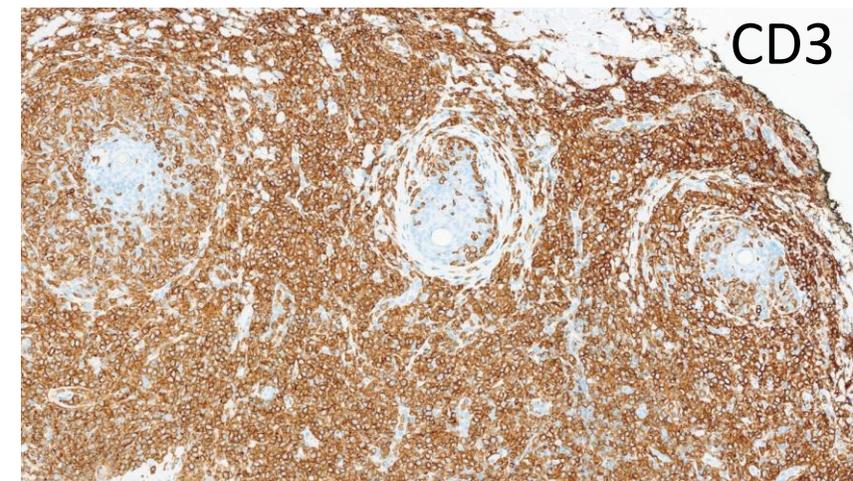
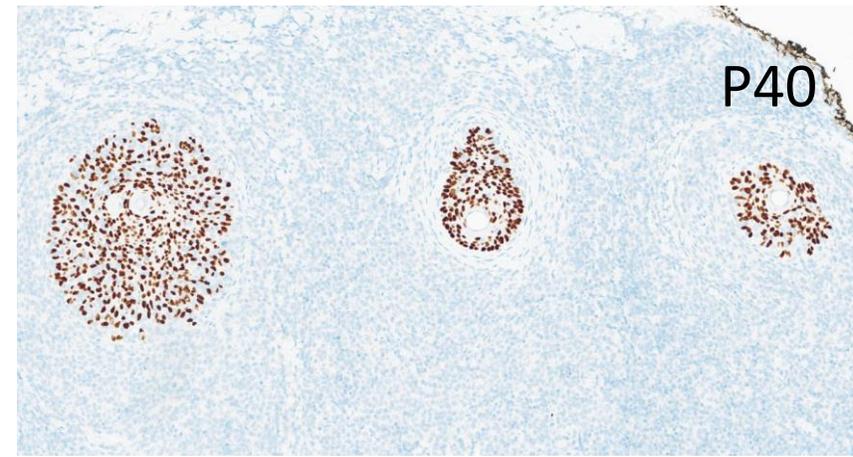
Punch biopsy of thigh lesion





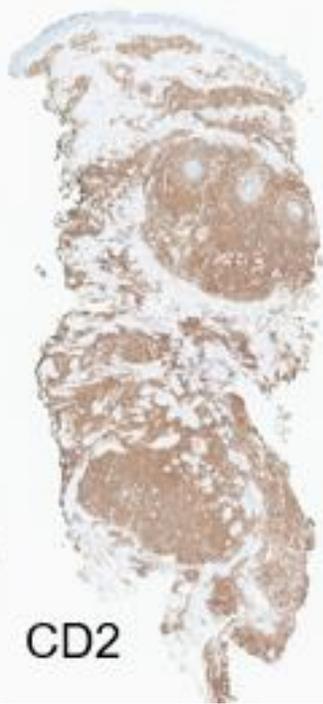








CD3



CD2



CD7



BF1



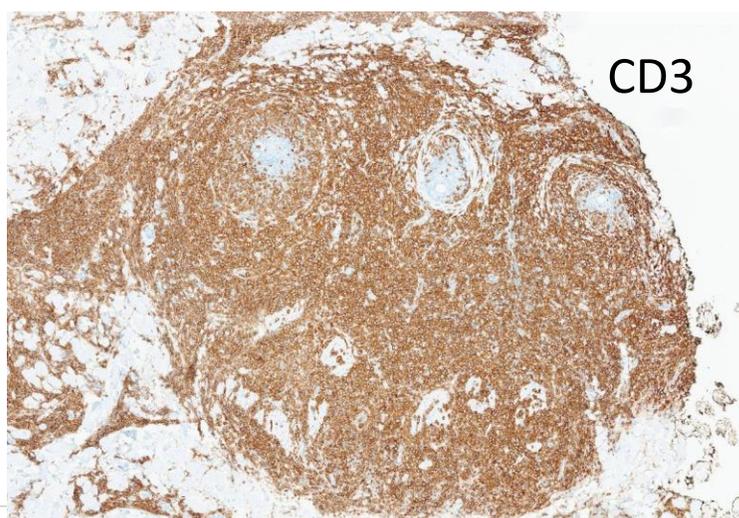
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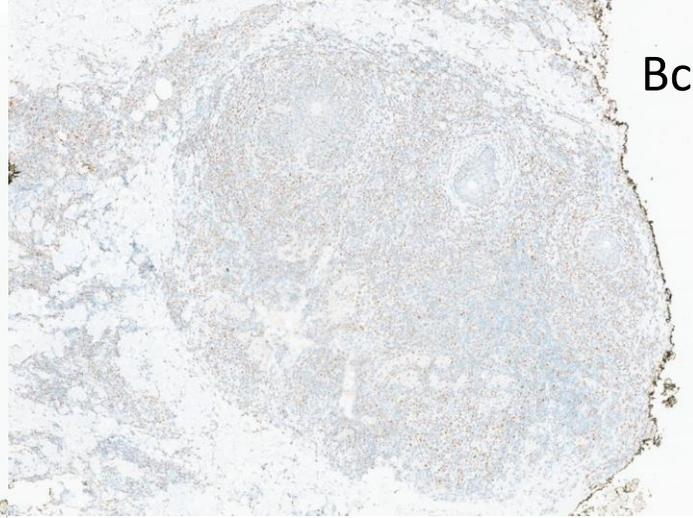
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CD20

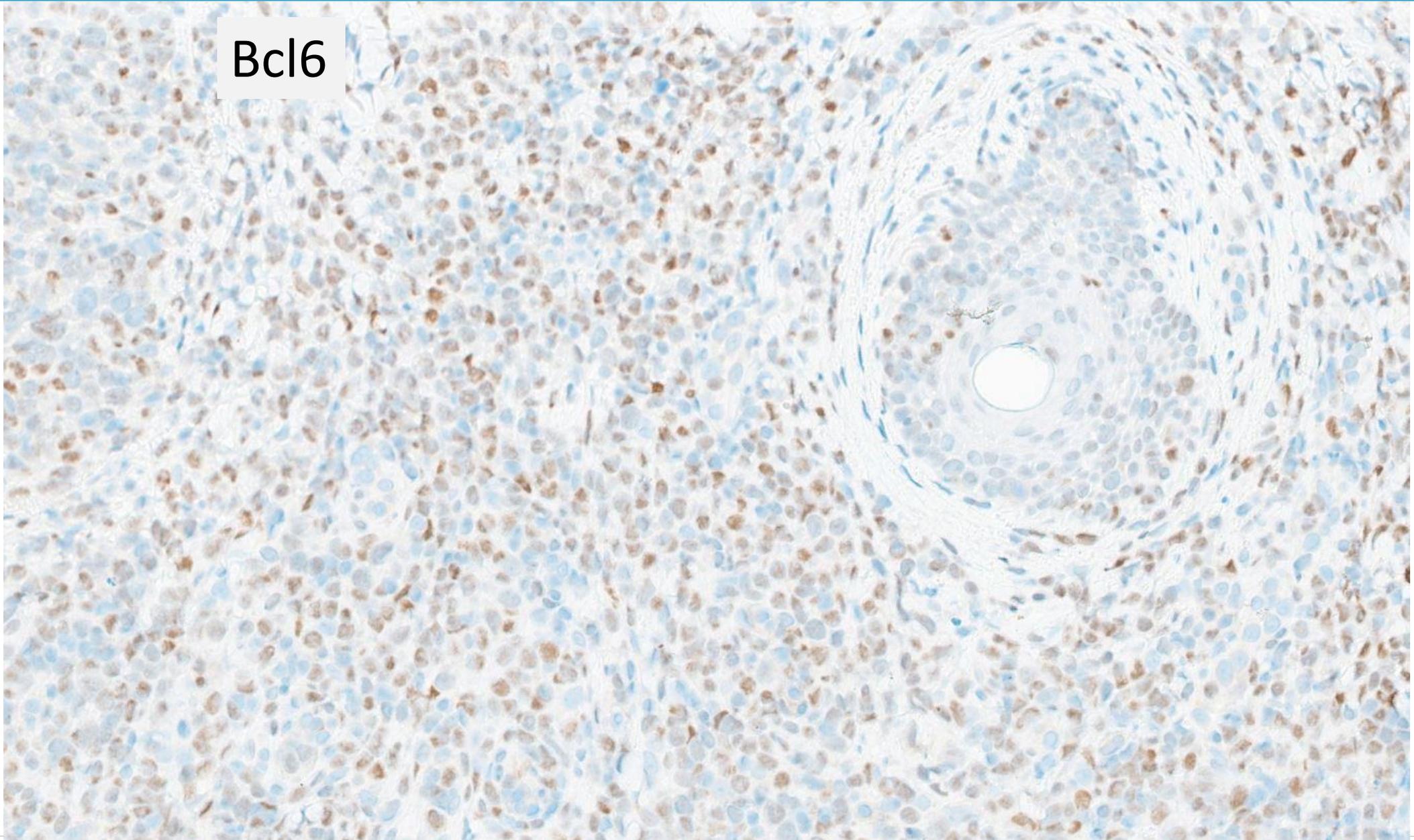


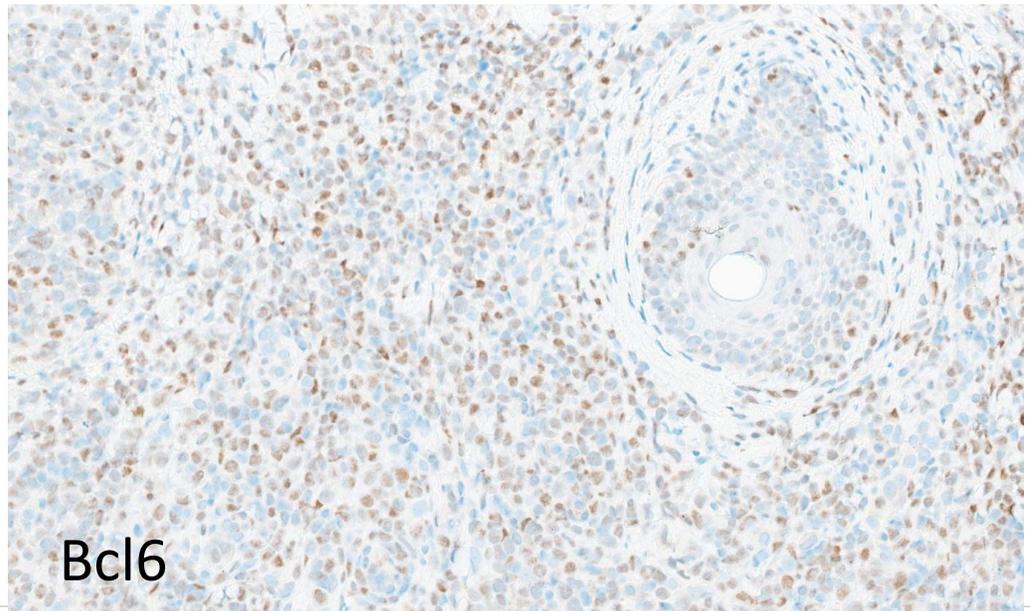
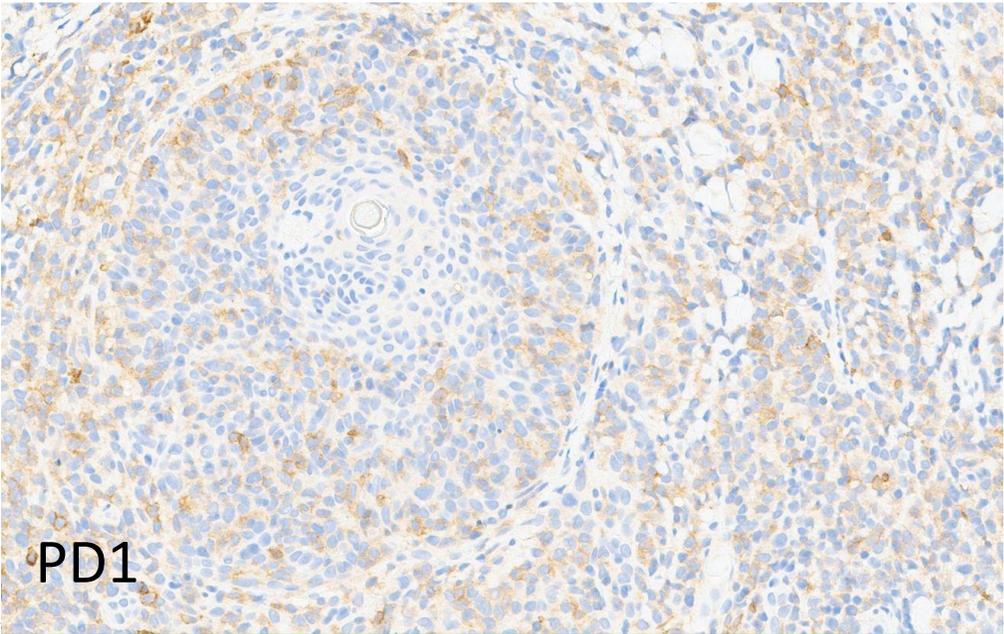
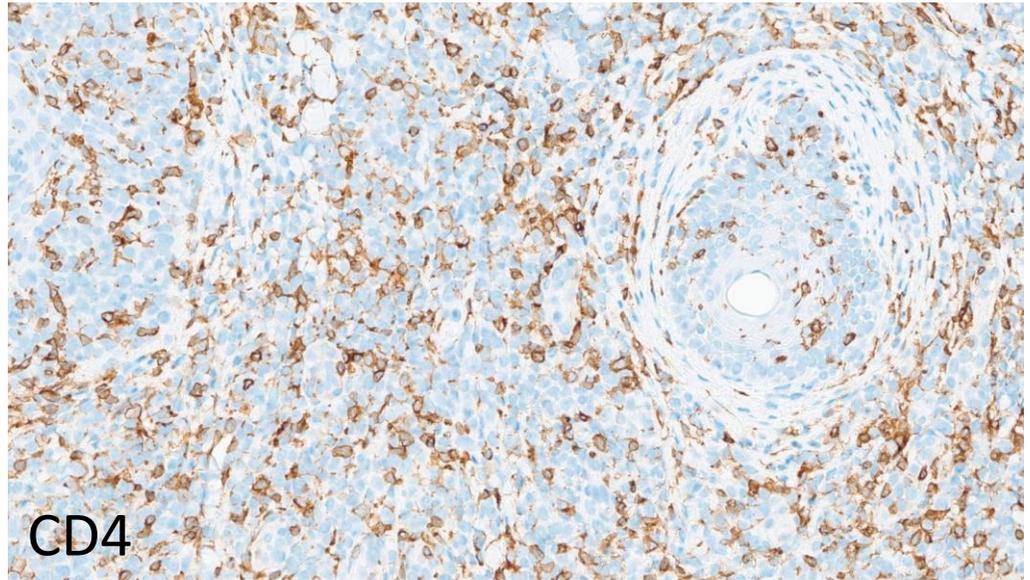
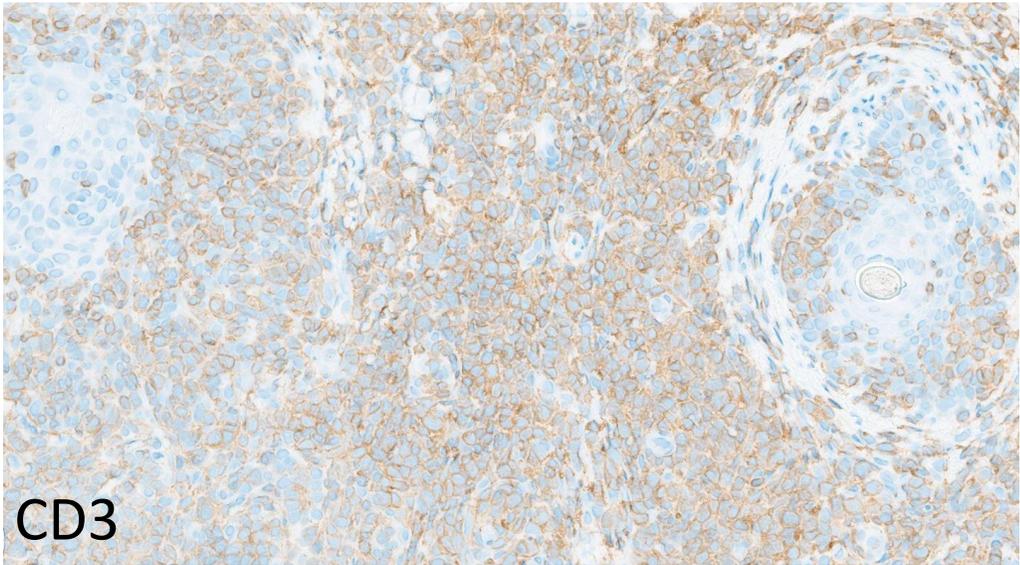
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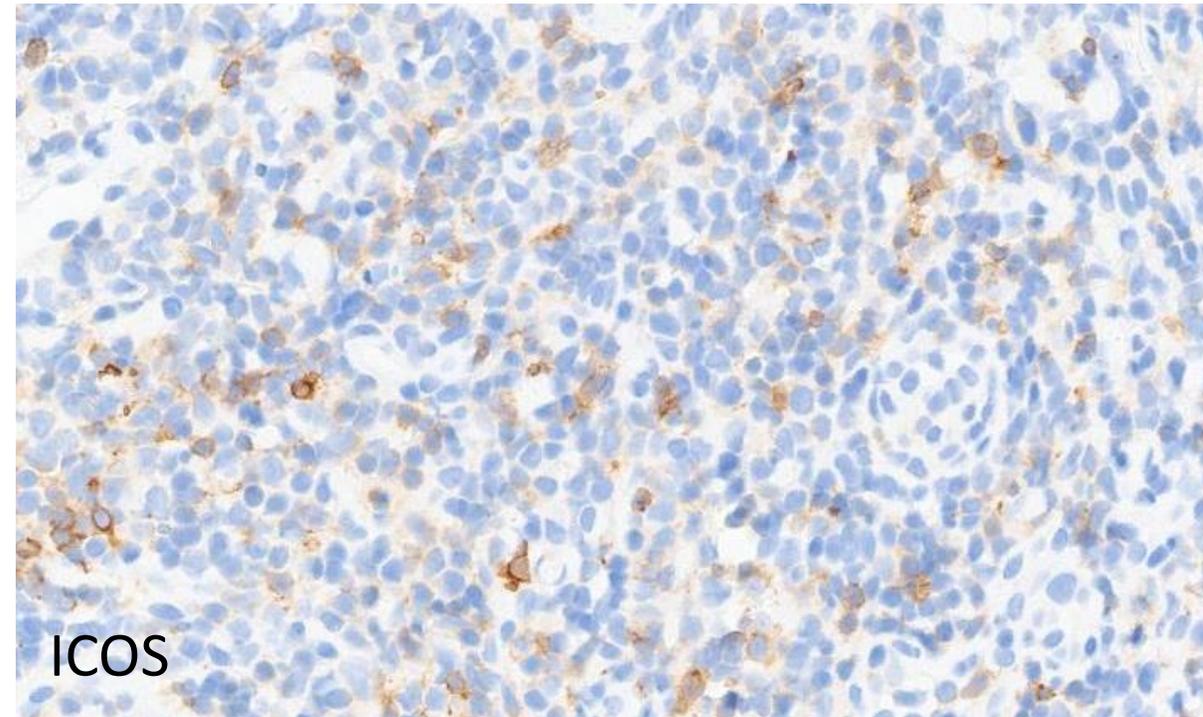
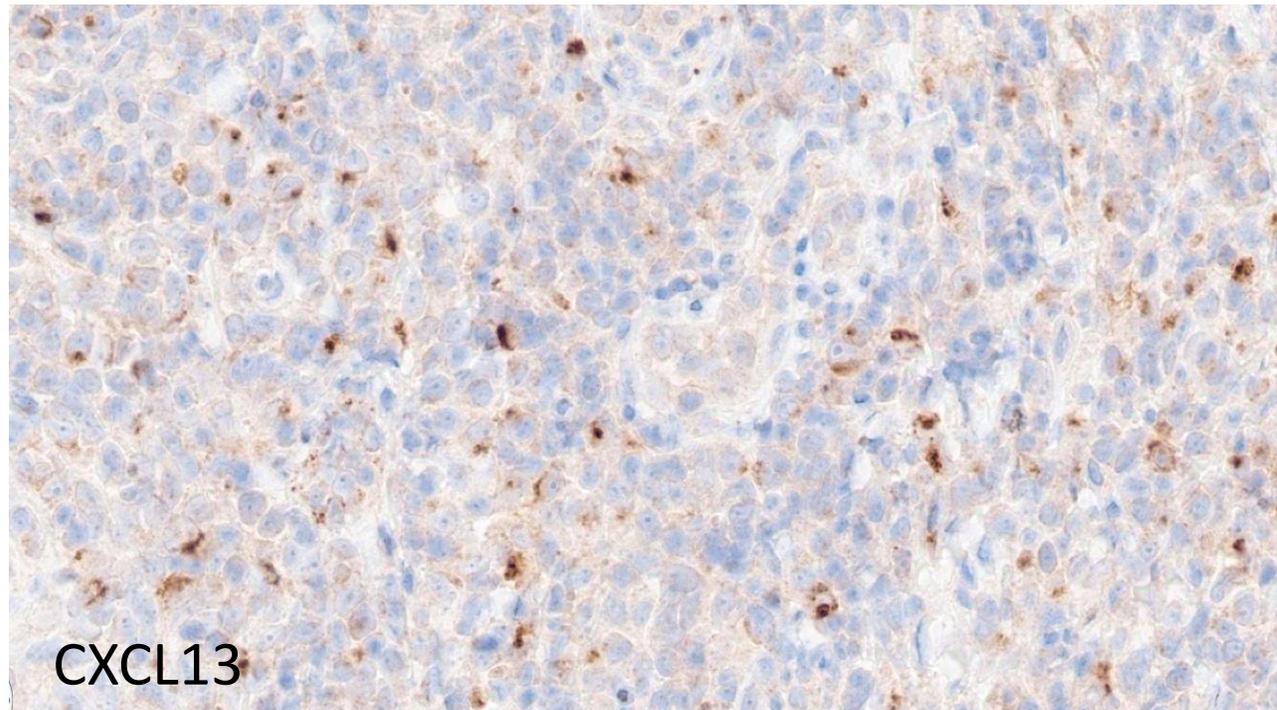


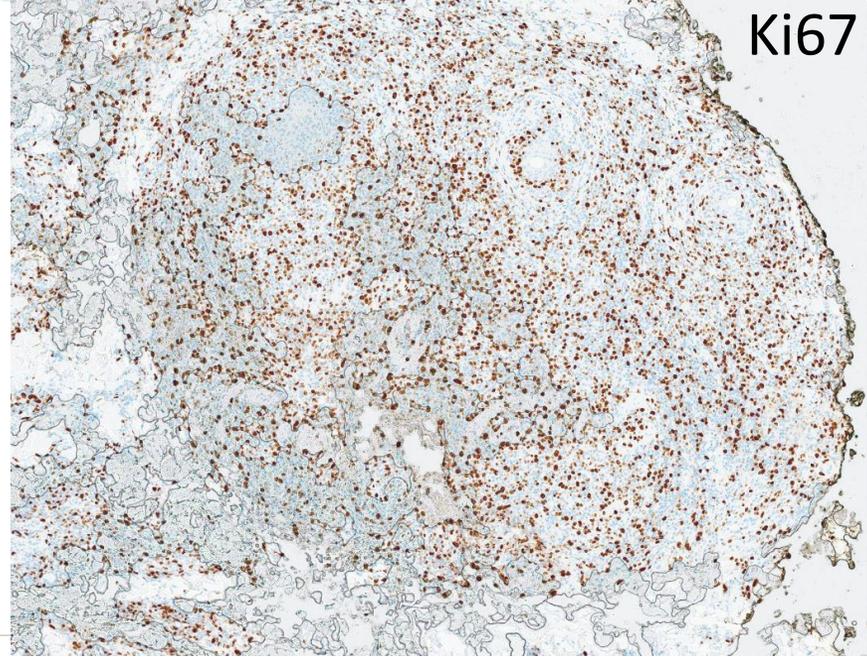
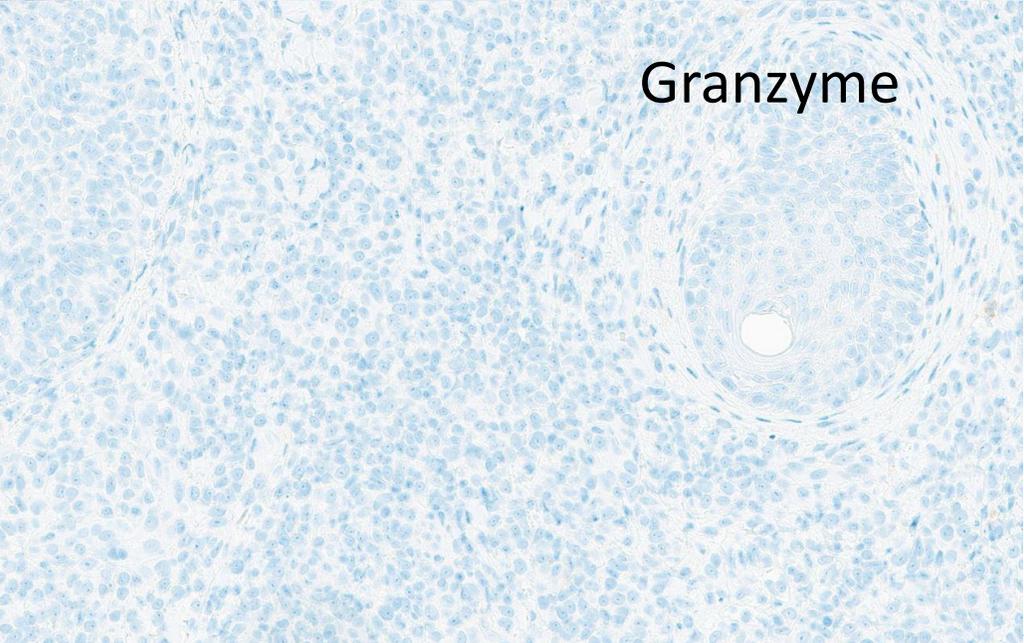
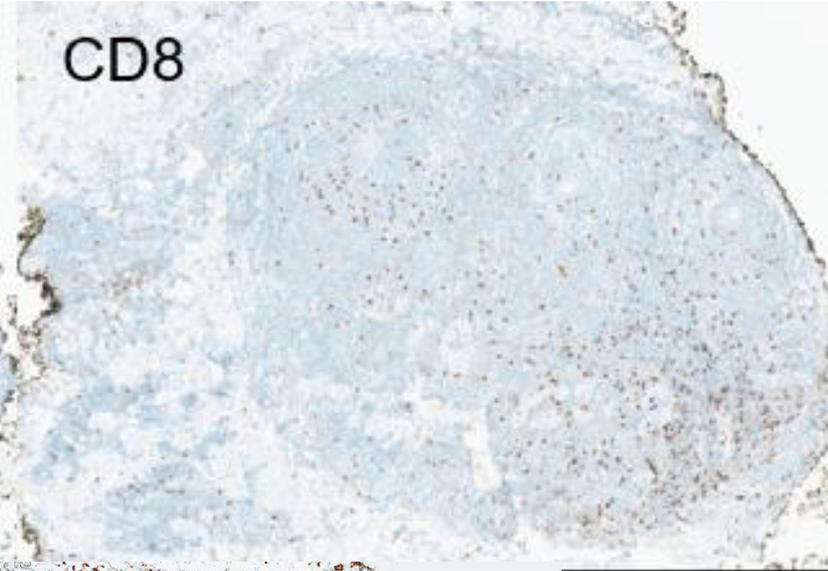
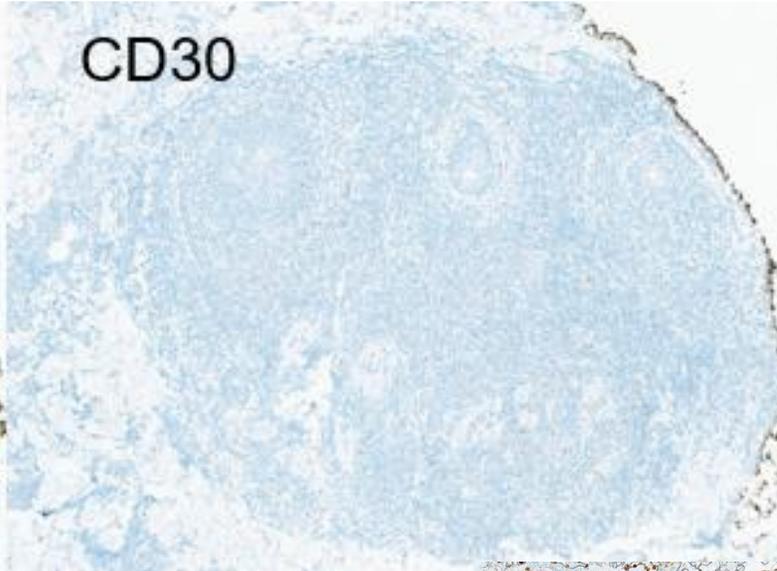
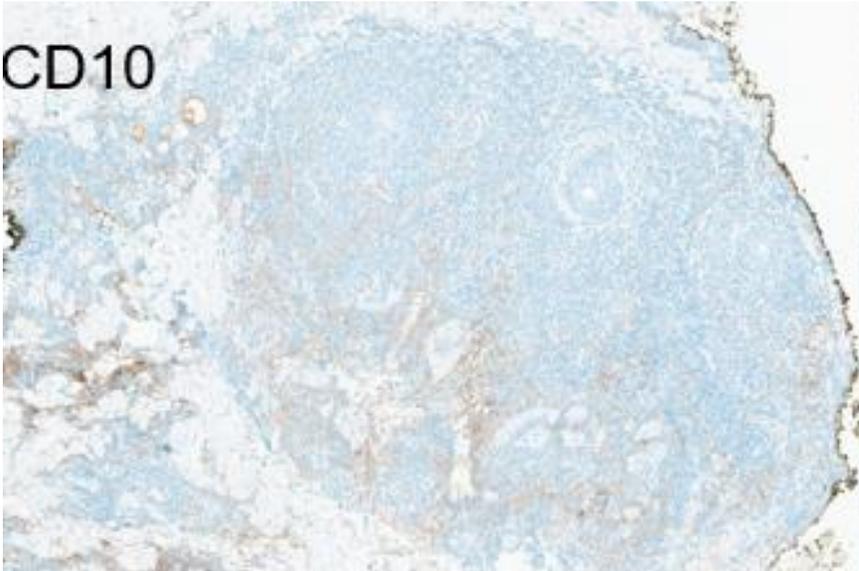
Bcl6

Bcl6

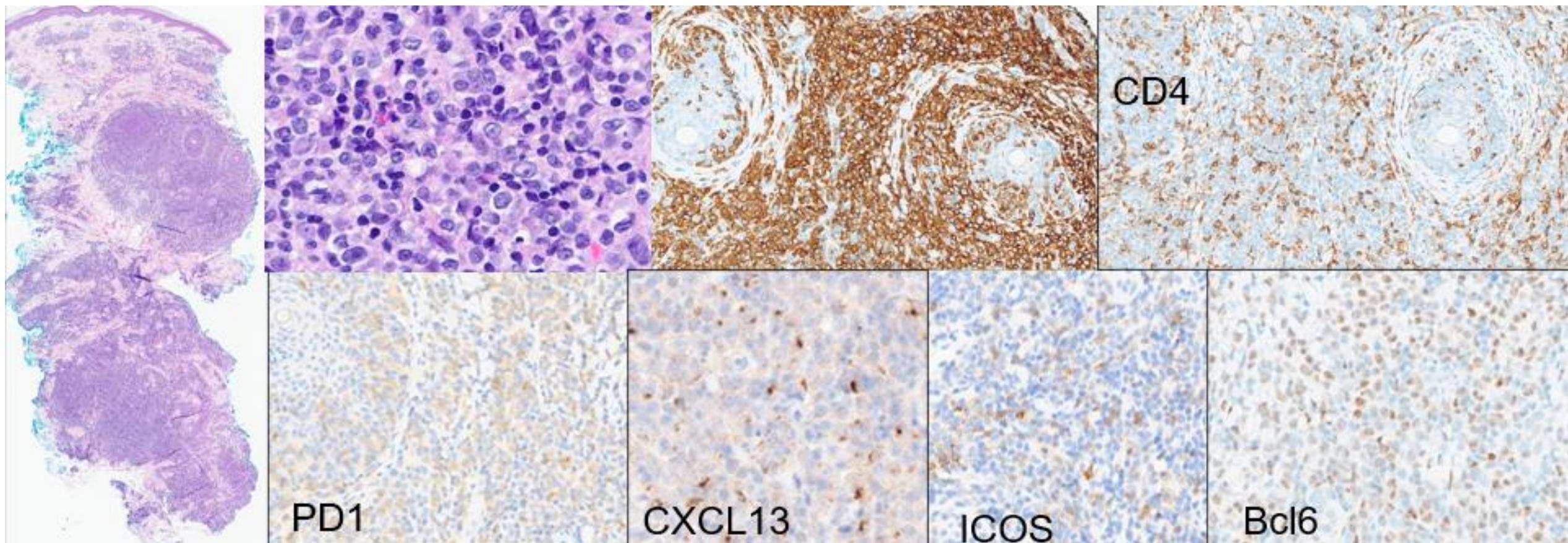




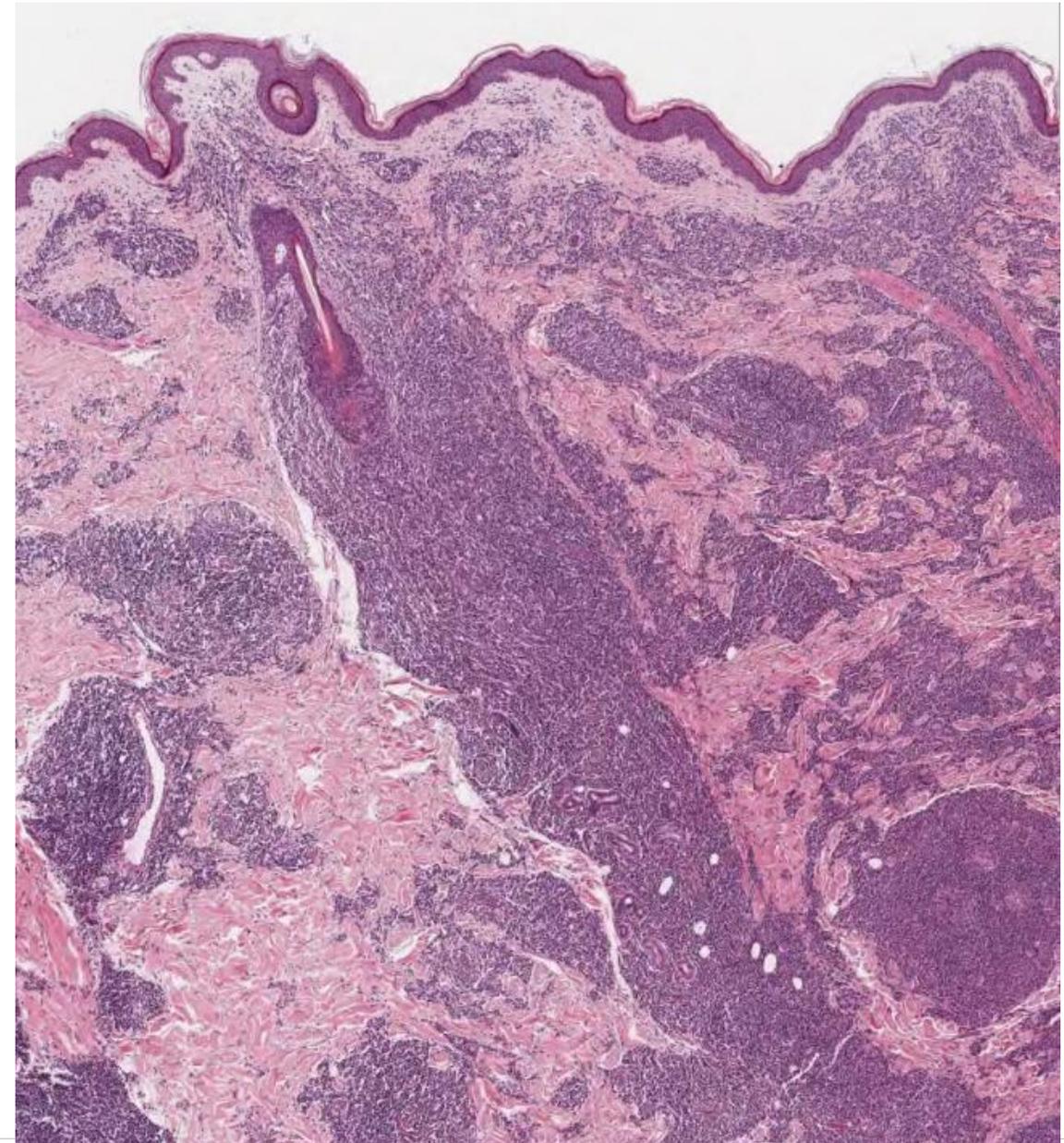
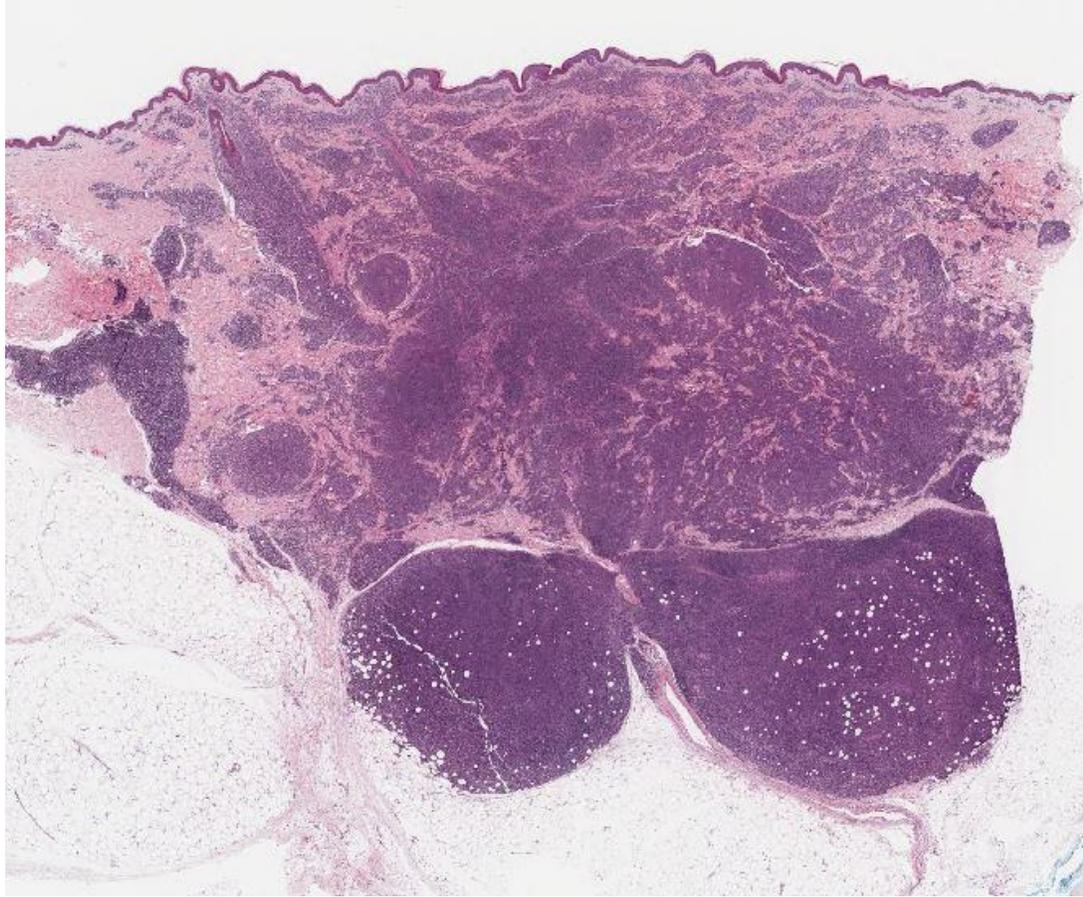


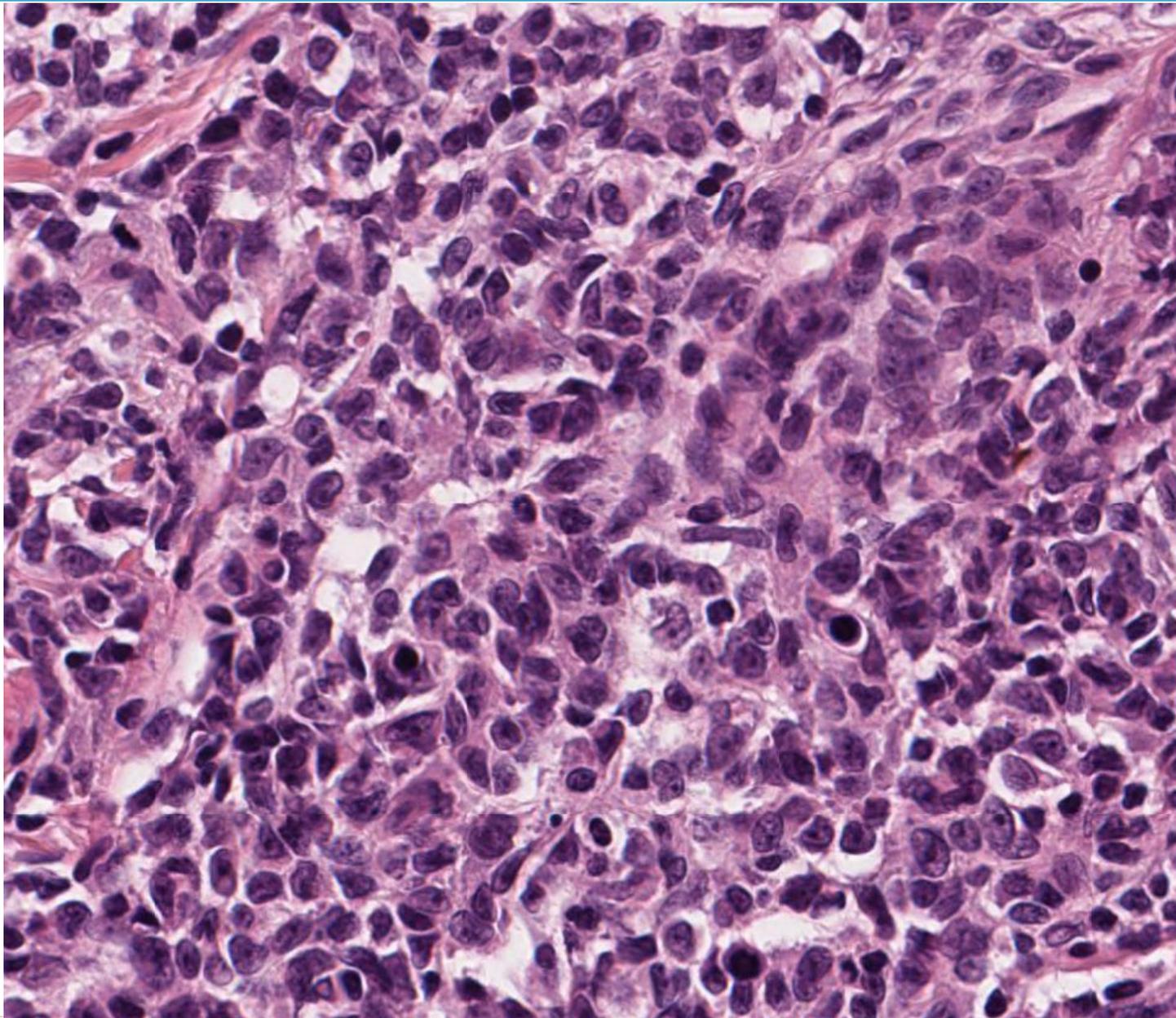


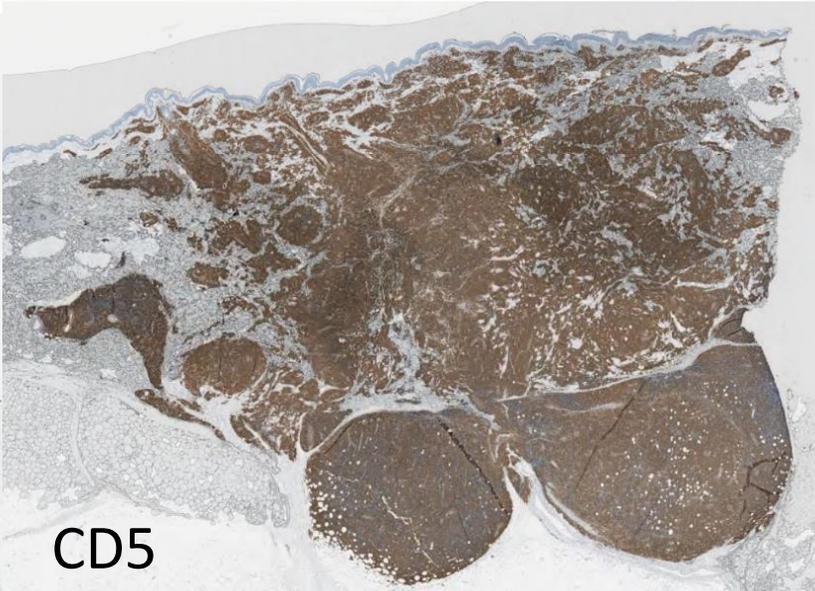
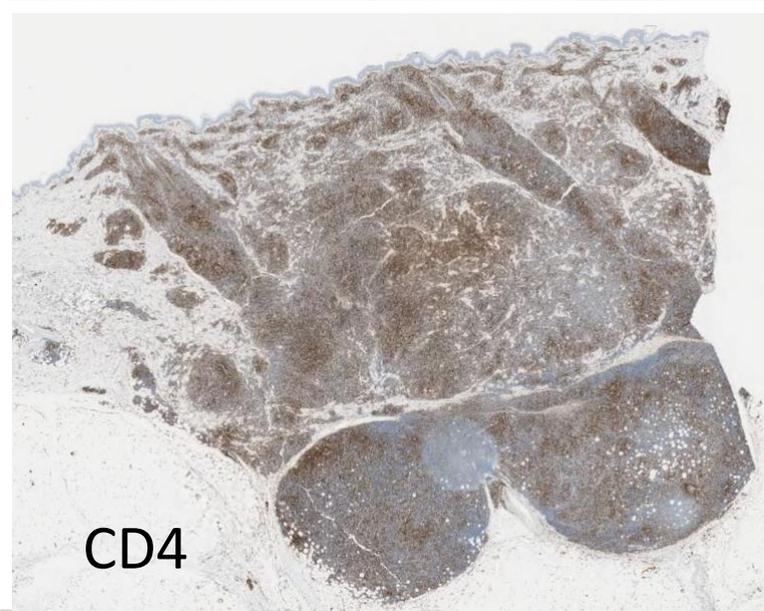
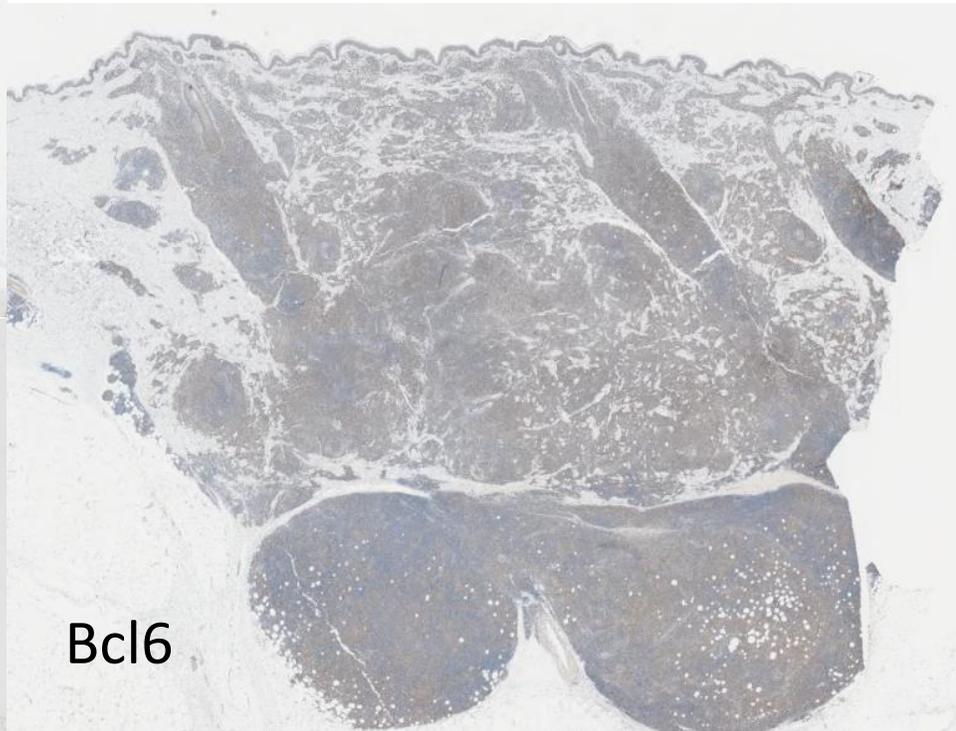
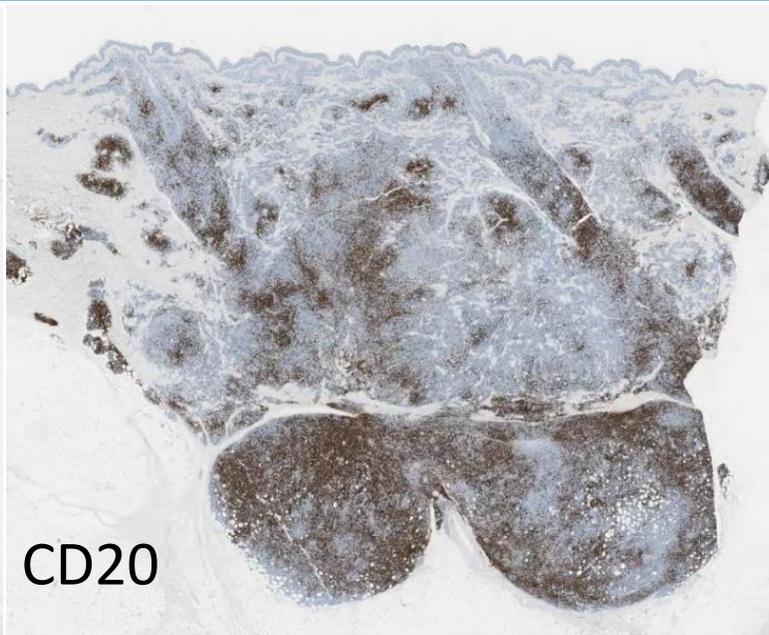
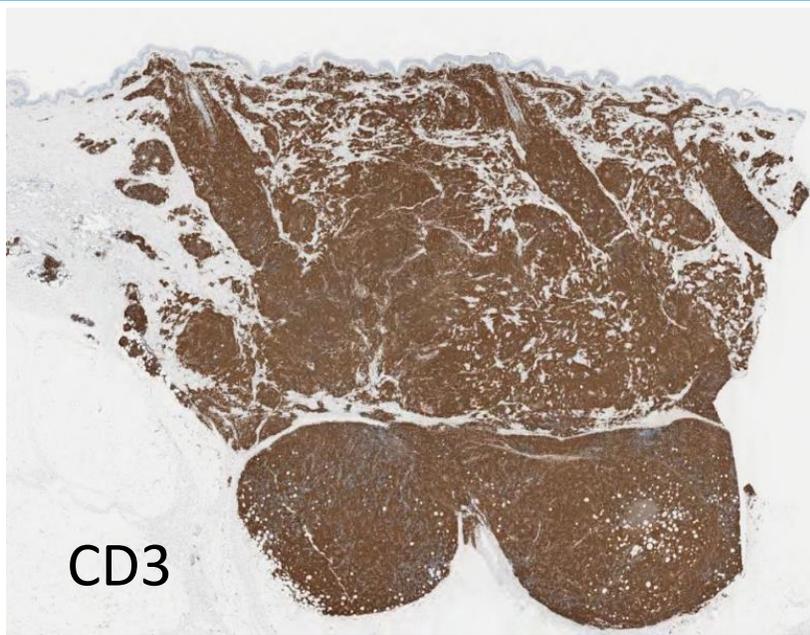
T cell lymphoma with T- follicular helper immunophenotype



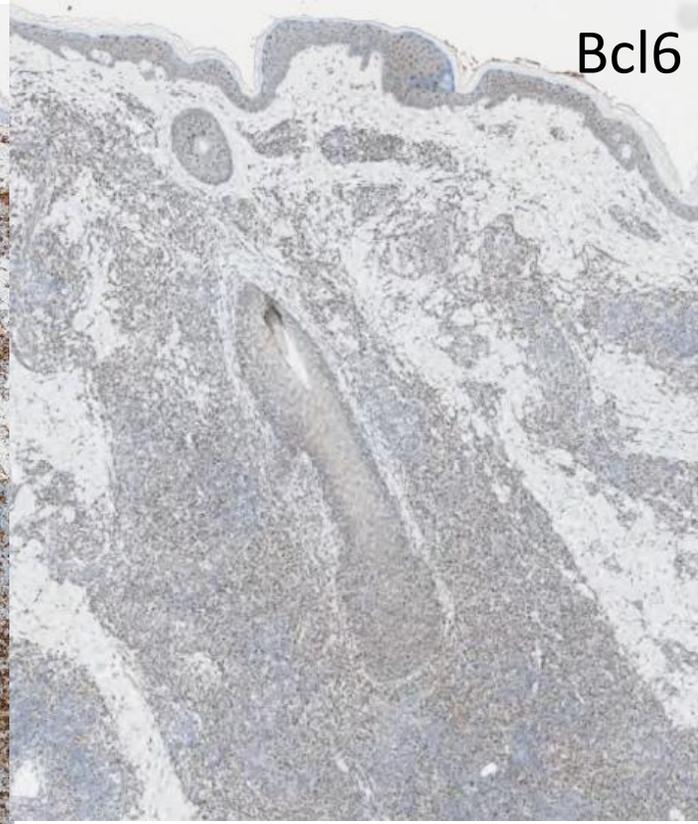
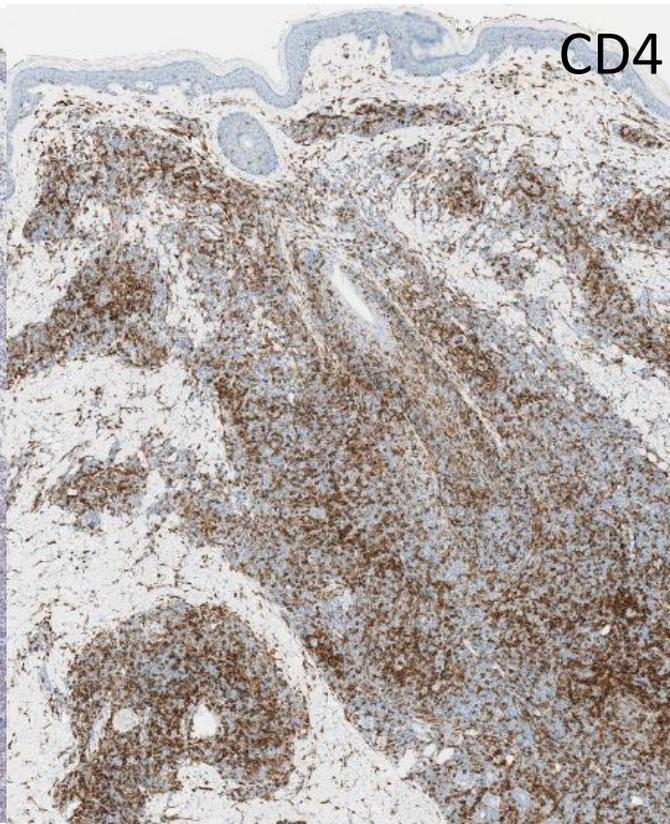
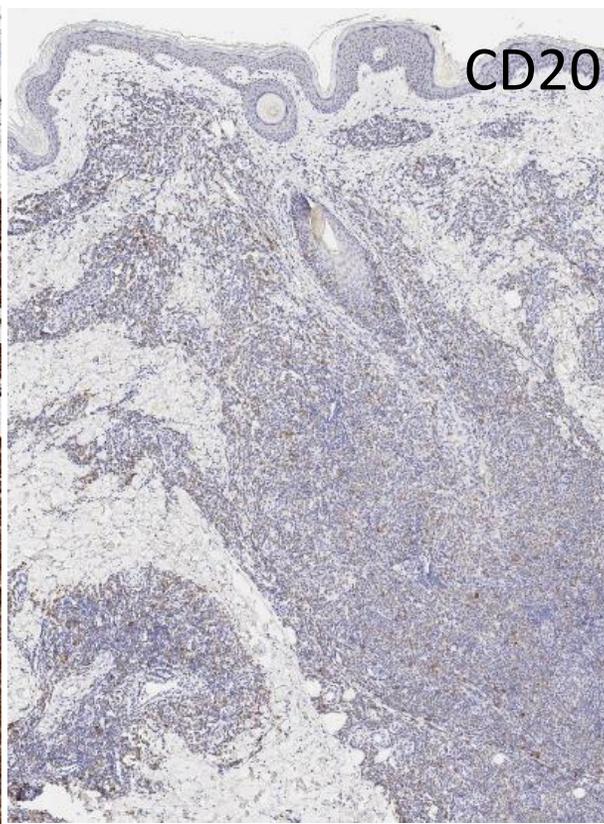
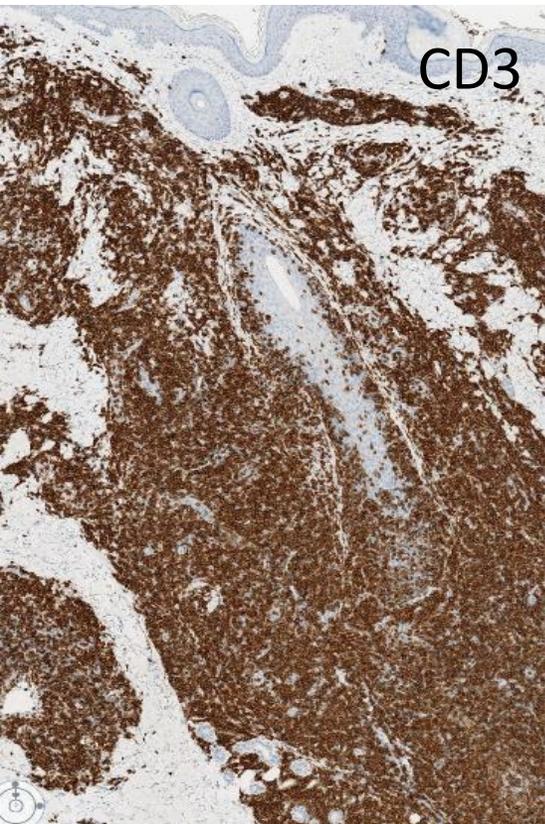
Tumor excision

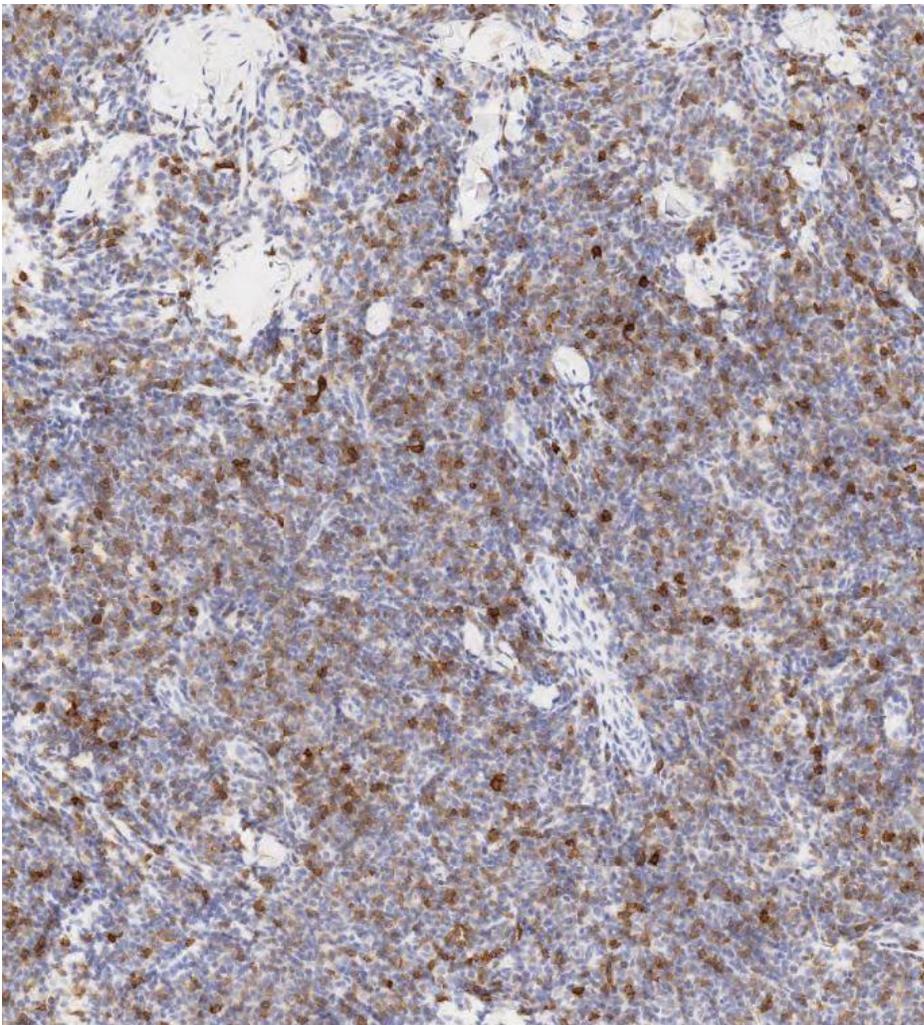




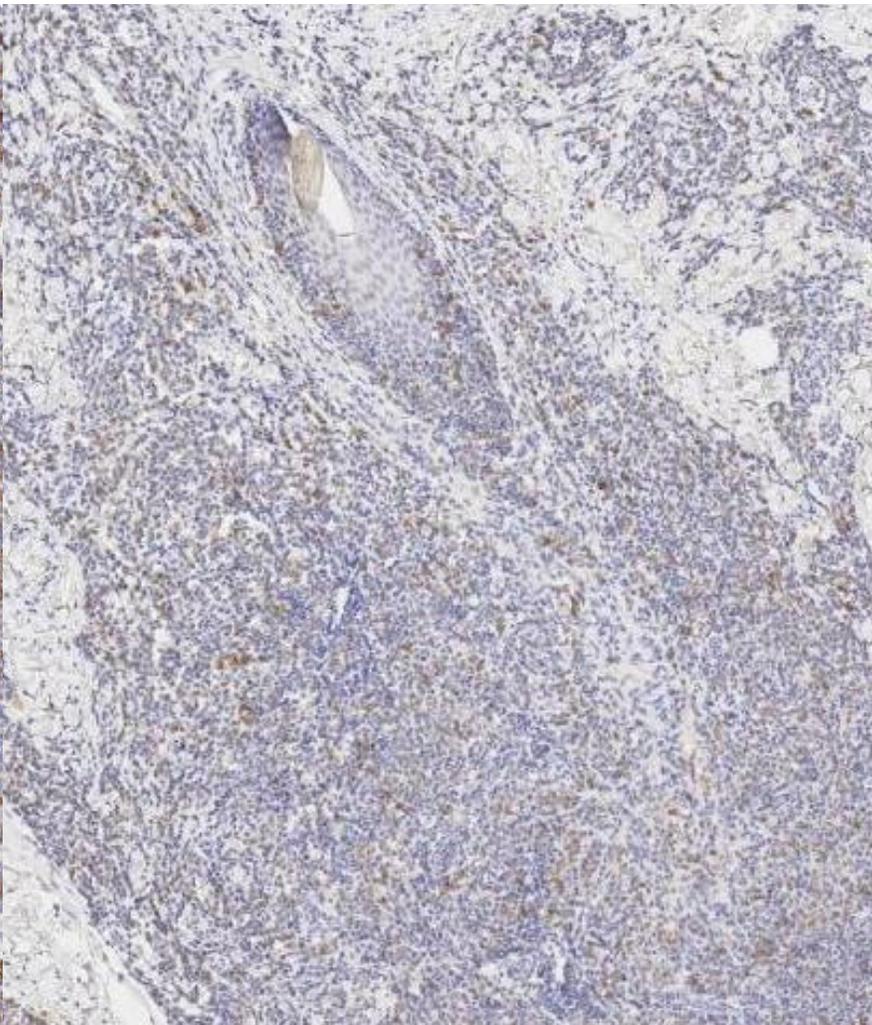


Folliculotropism

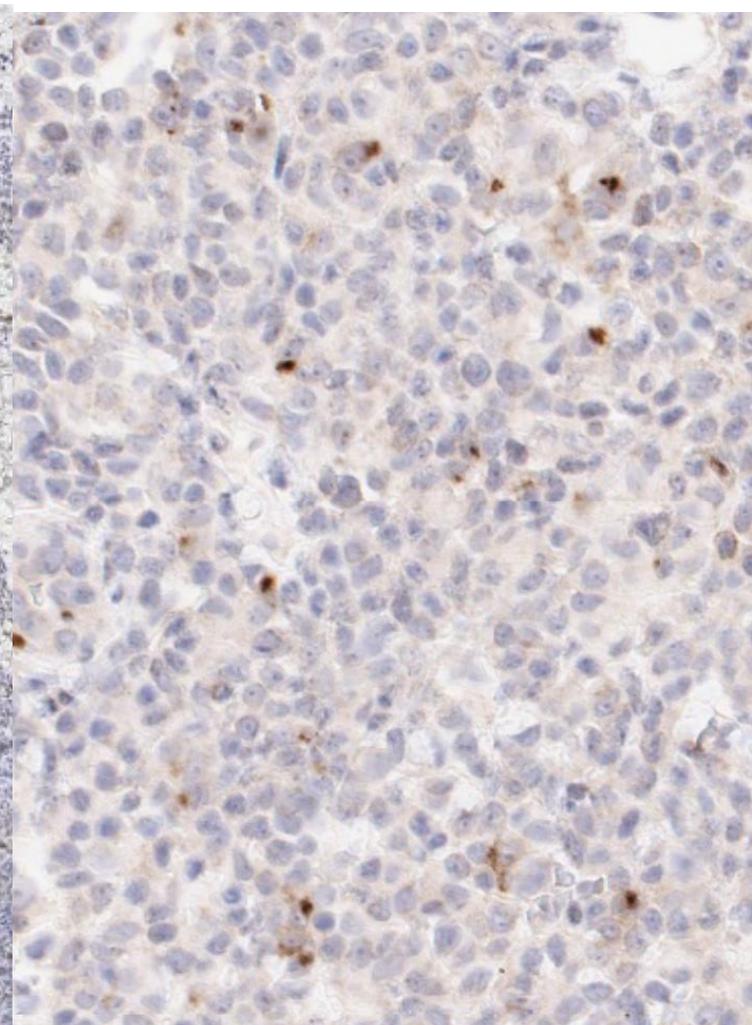




ICOS

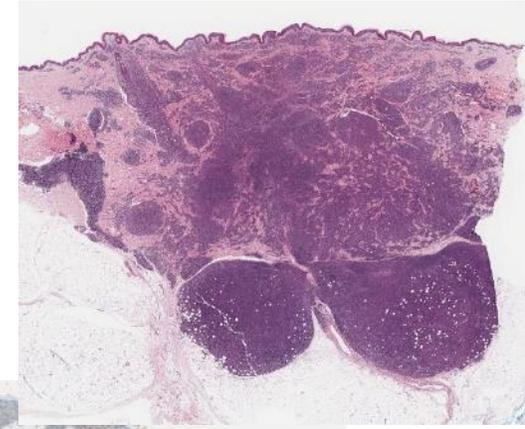
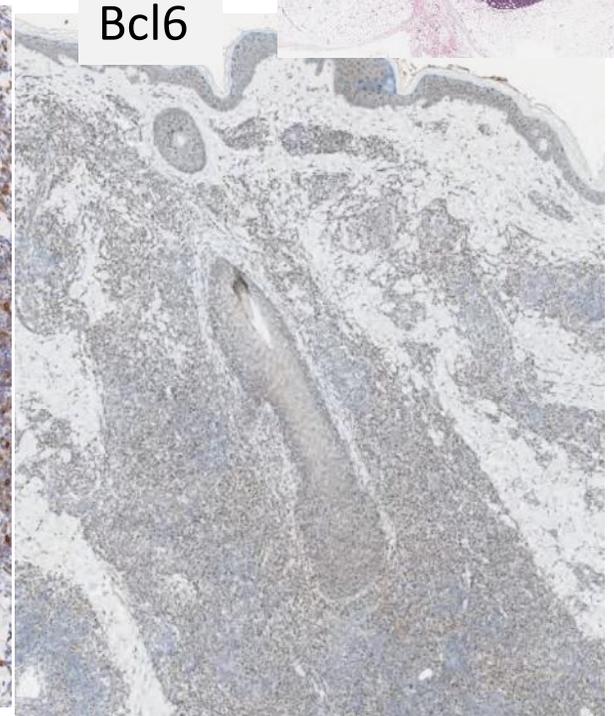
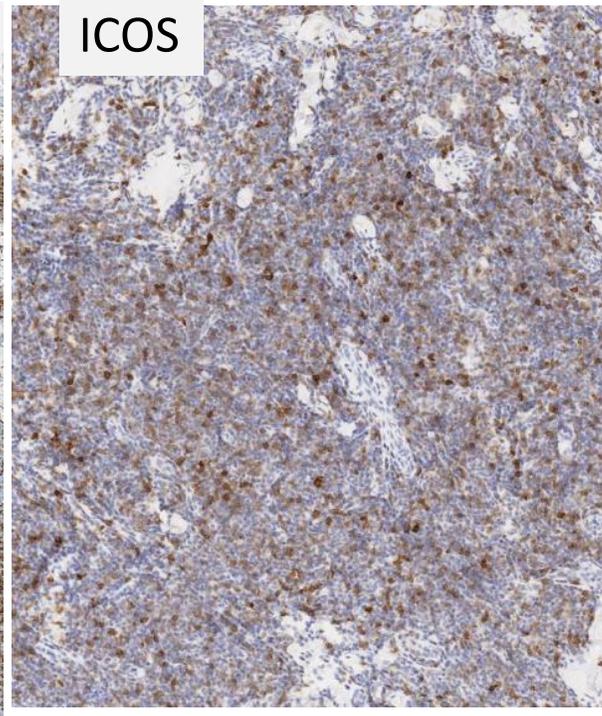
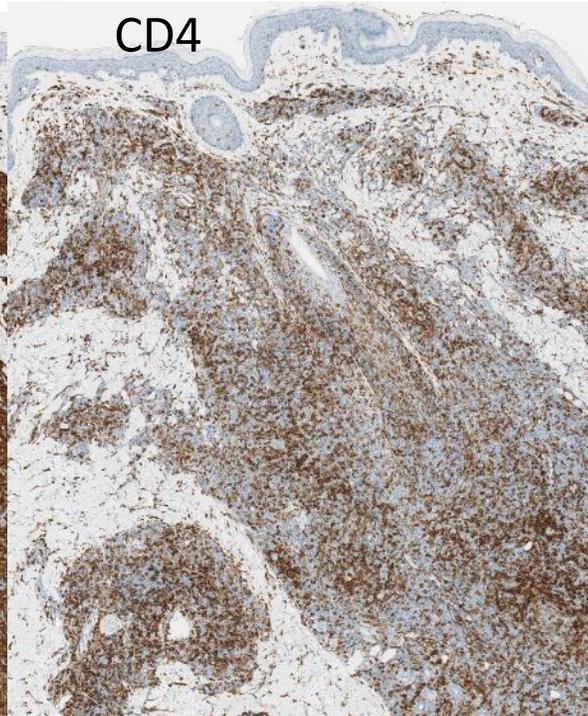
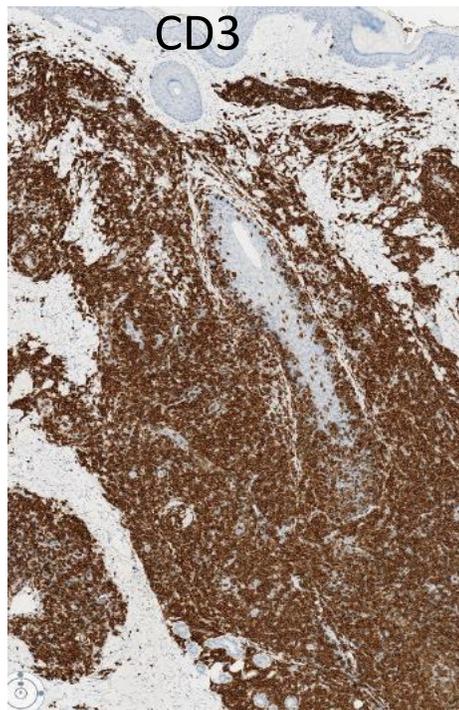


PD1



CXCL13

Primary cutaneous follicular helper T cell lymphoma

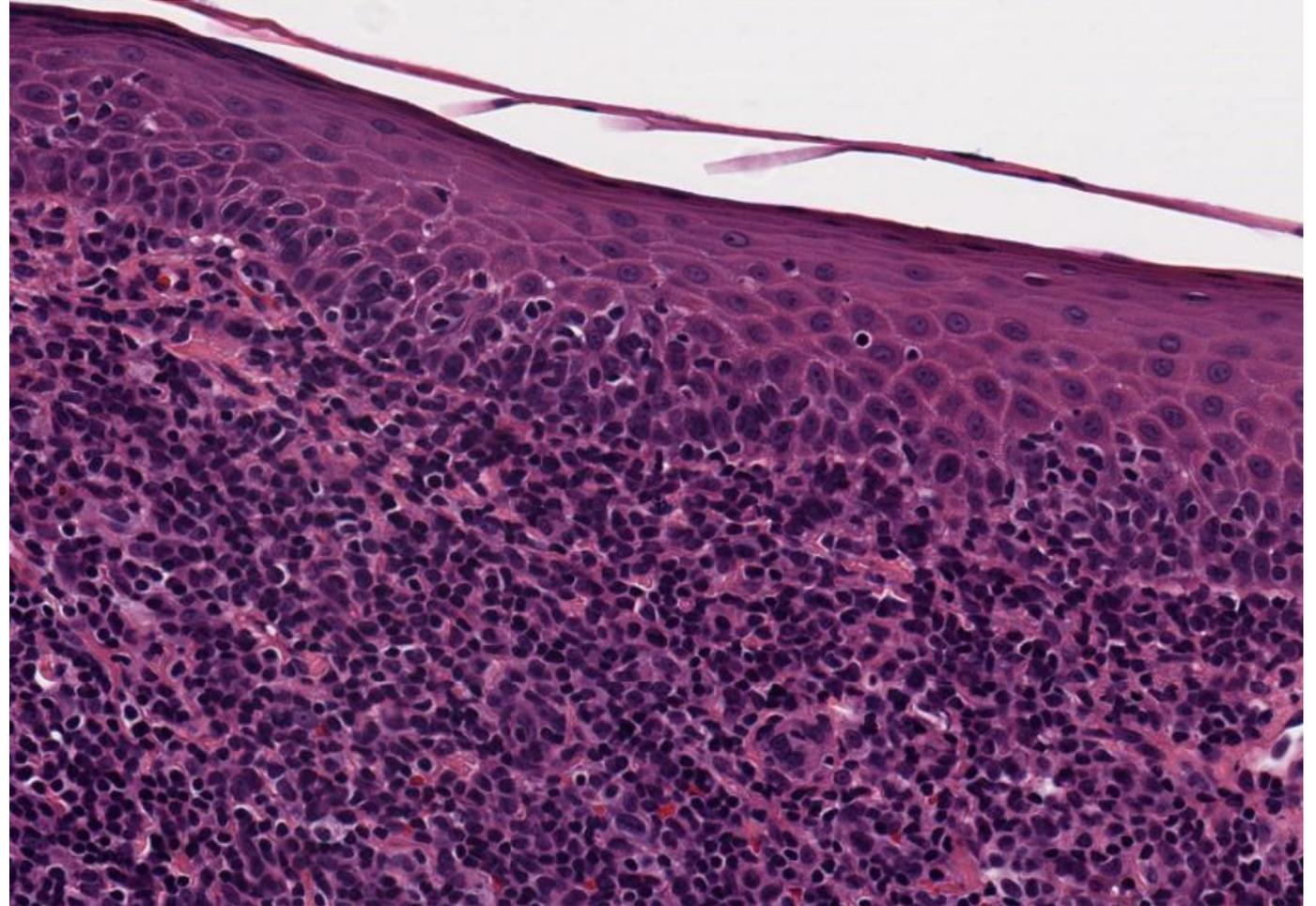
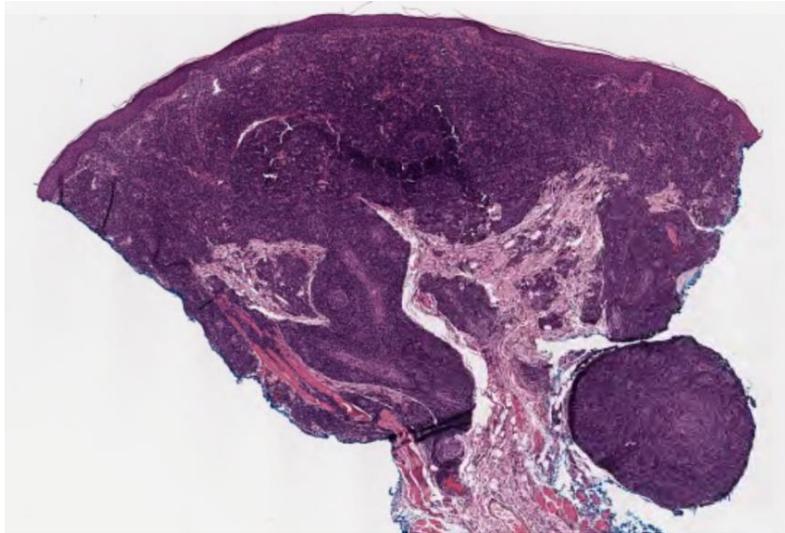


+ CD3/CD4/Bcl6/PD1/ICOS/CXCL13
(-) EBER/CD30/CD10

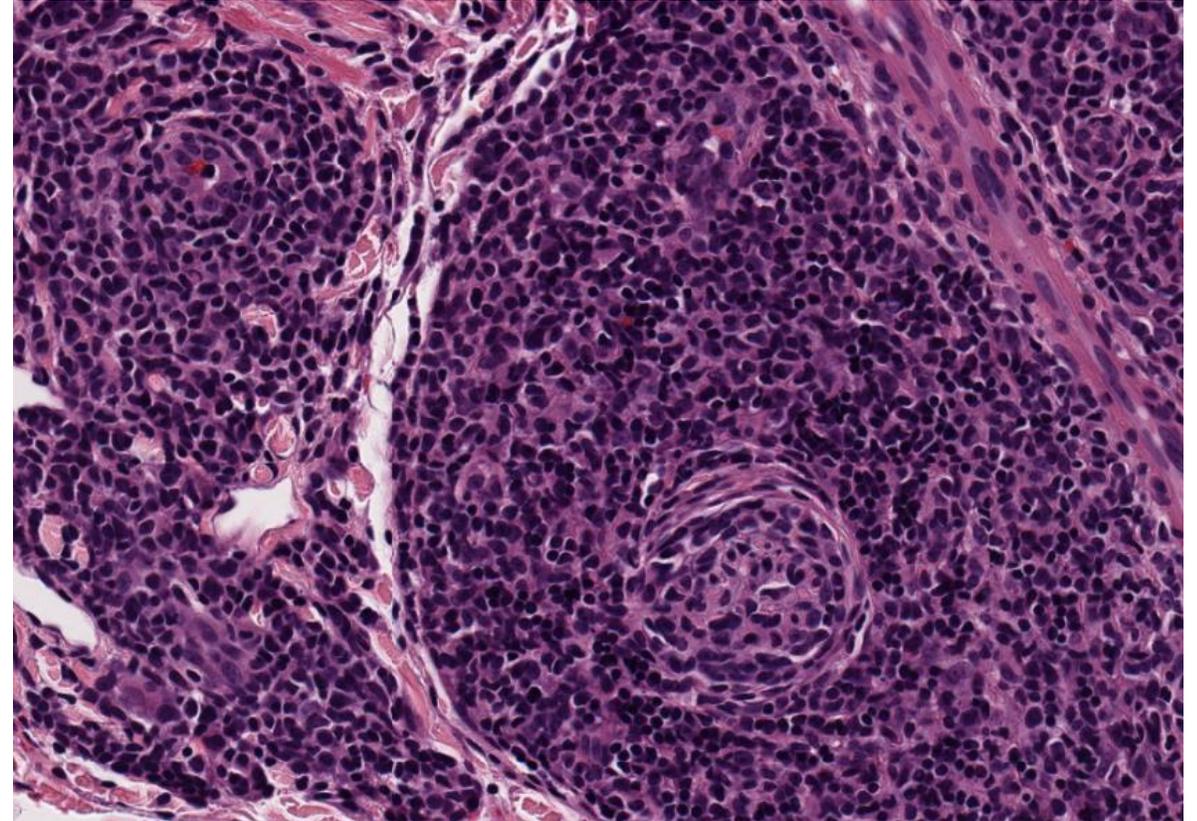
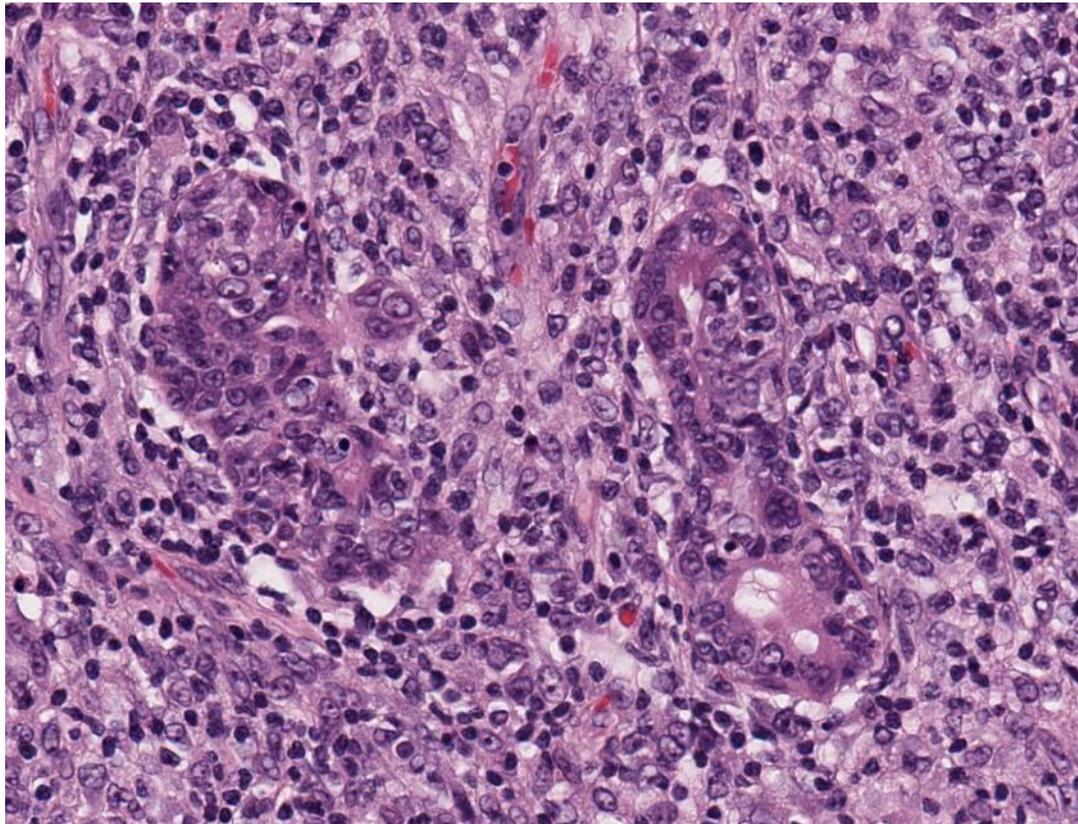
(-) Systemic work up (PET/CT, bone marrow, and flow)



Tumor, lip



Syringotropic, vasculocentric

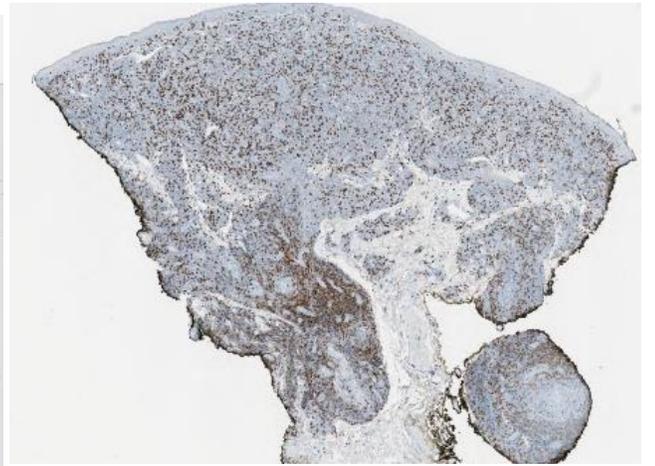
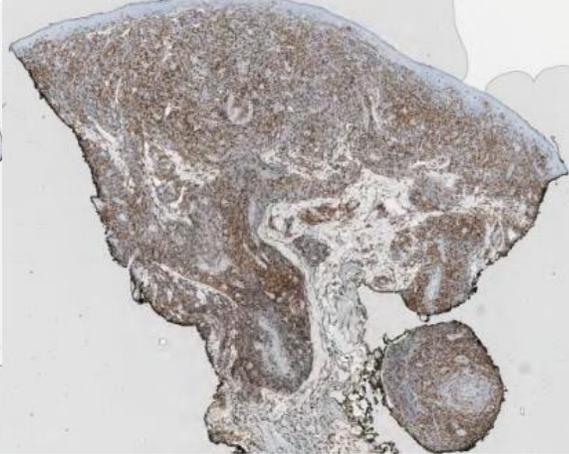
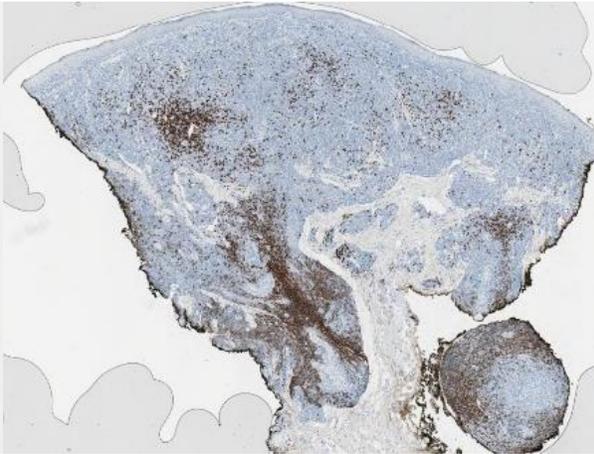


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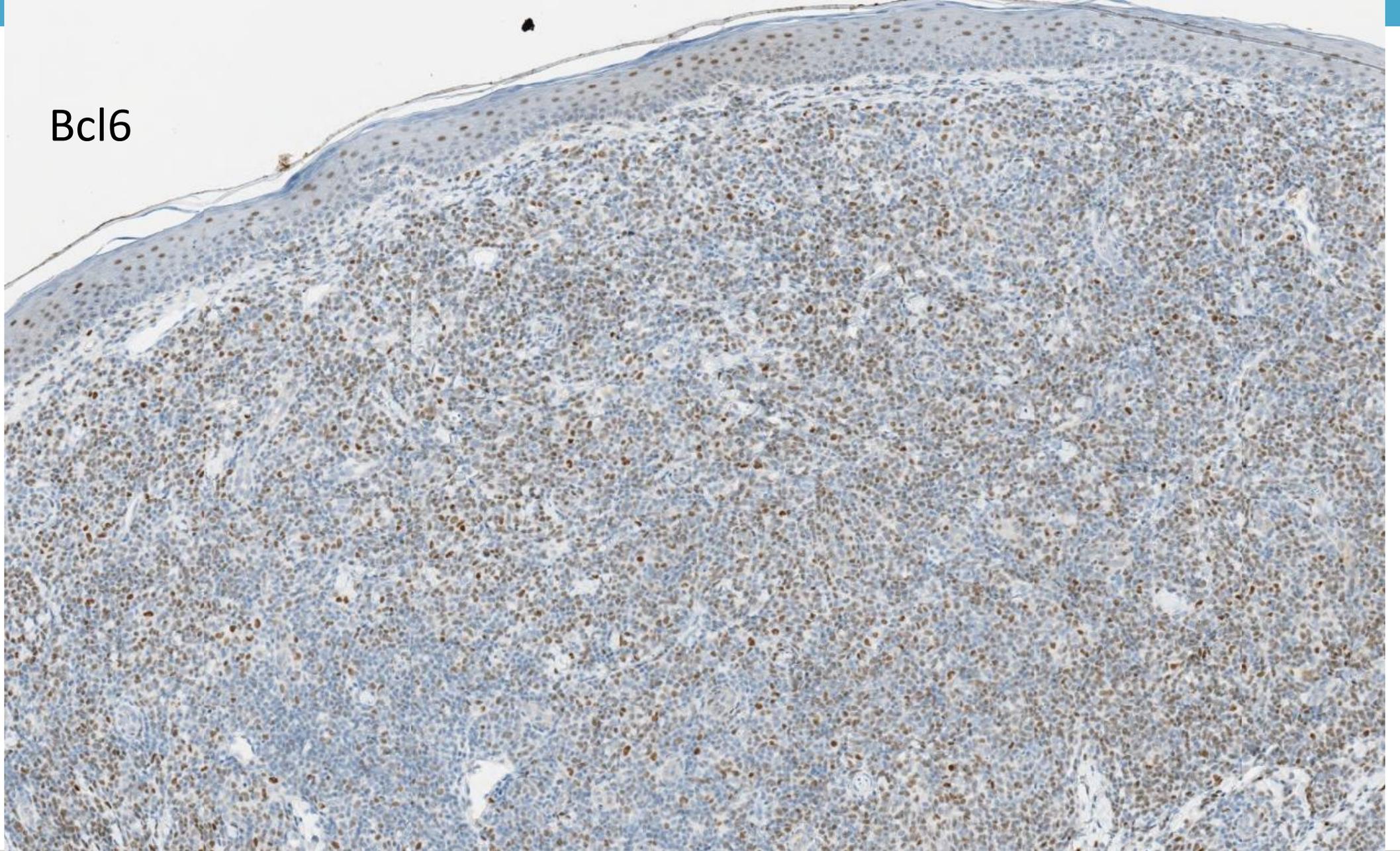
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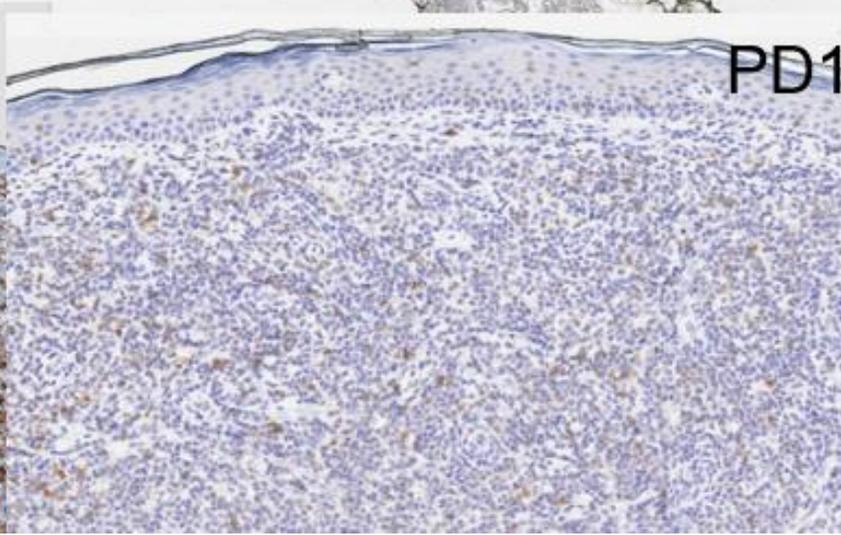
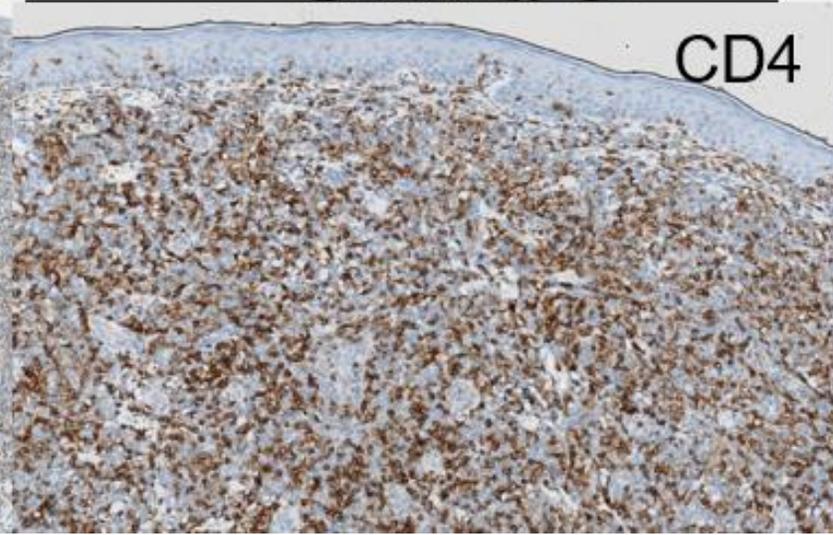
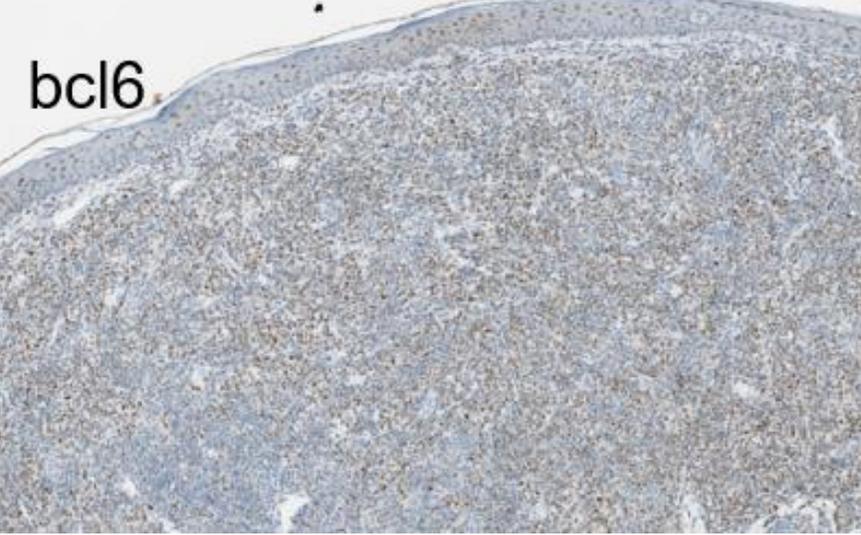
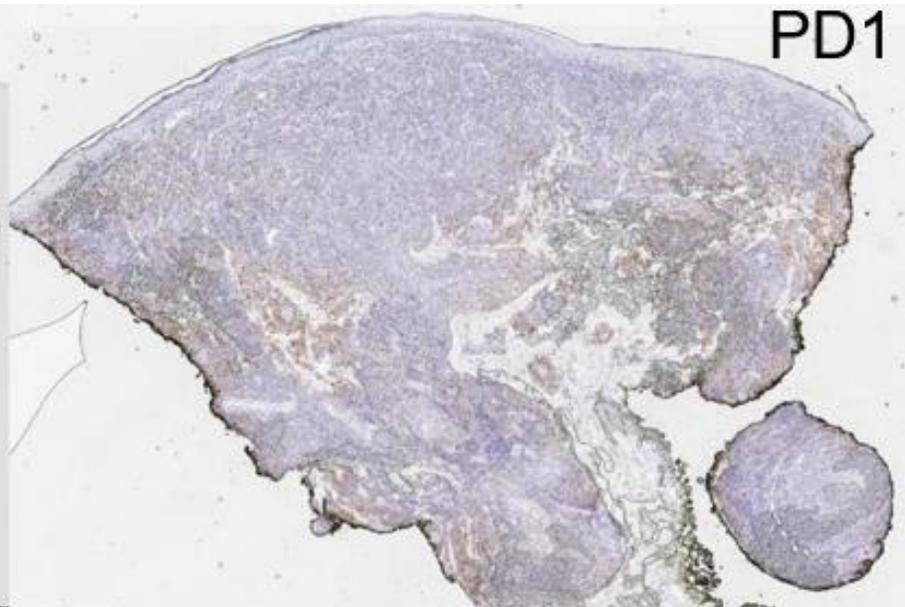
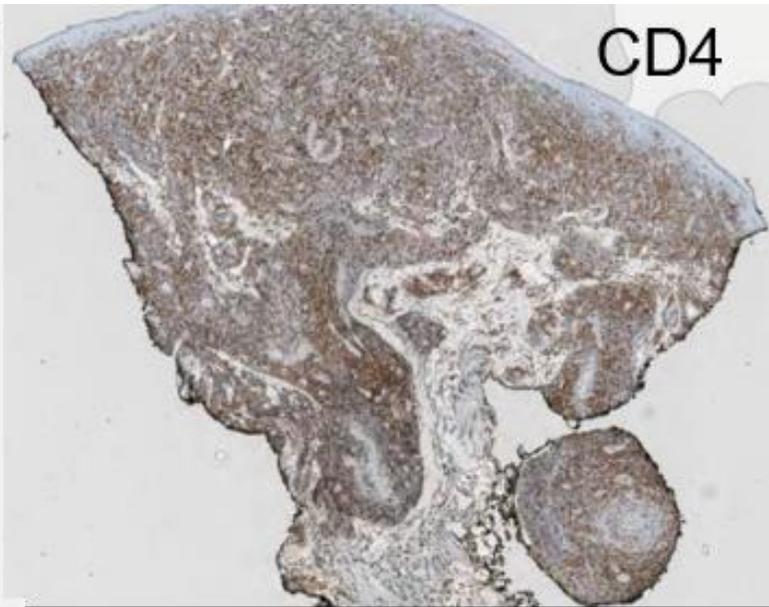
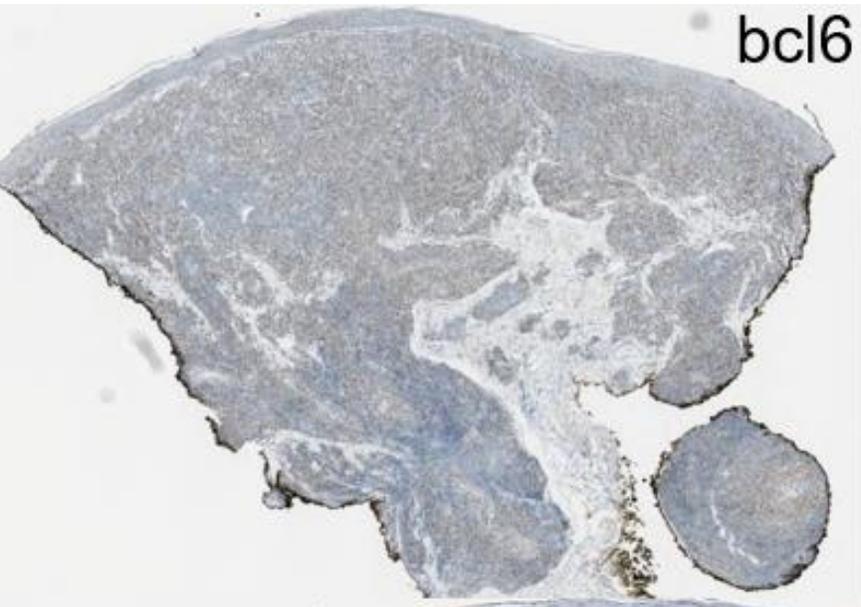
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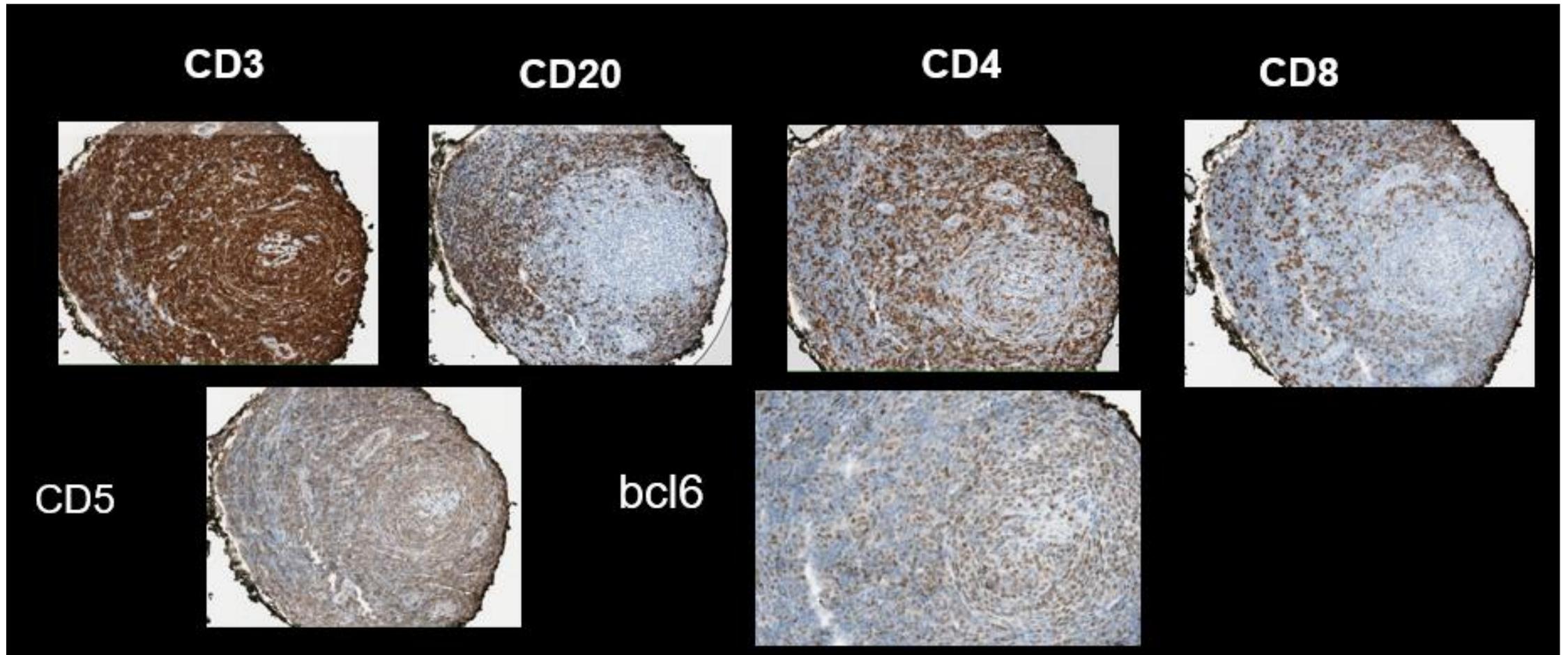


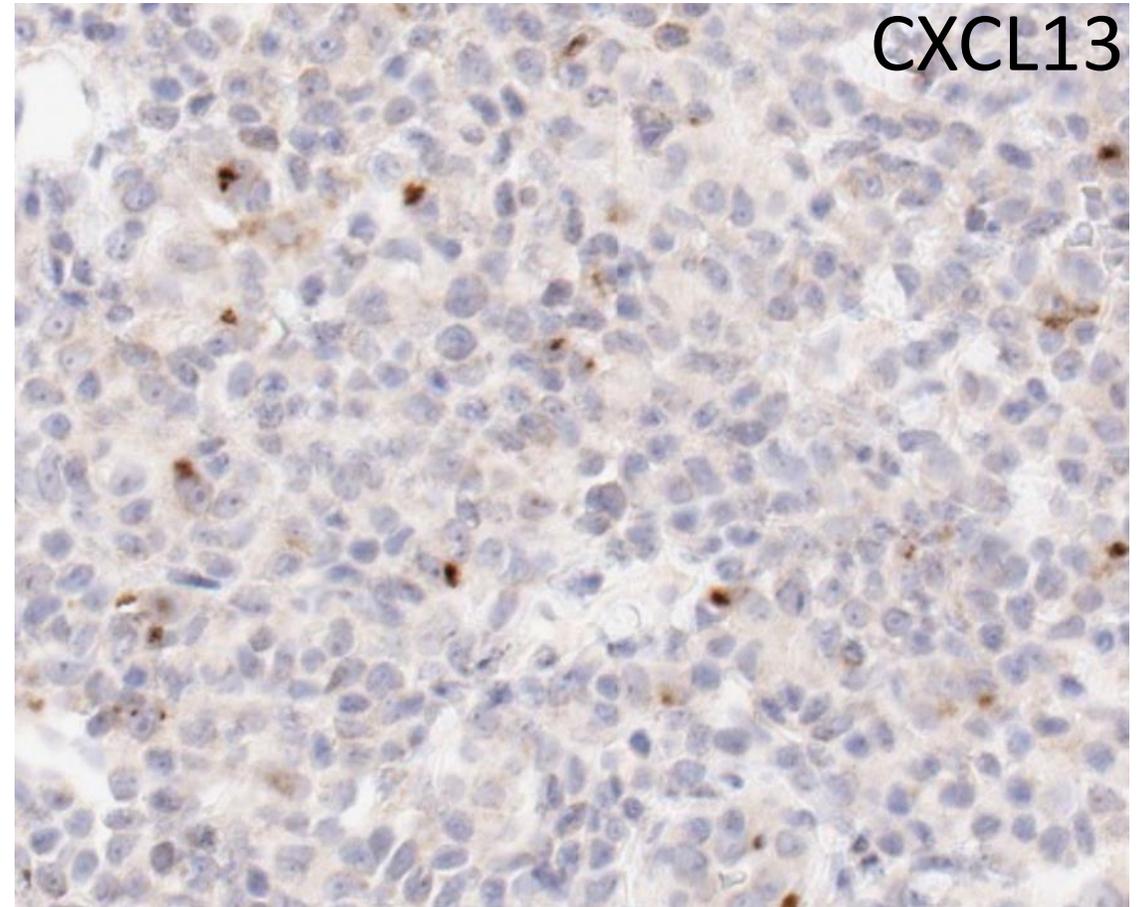
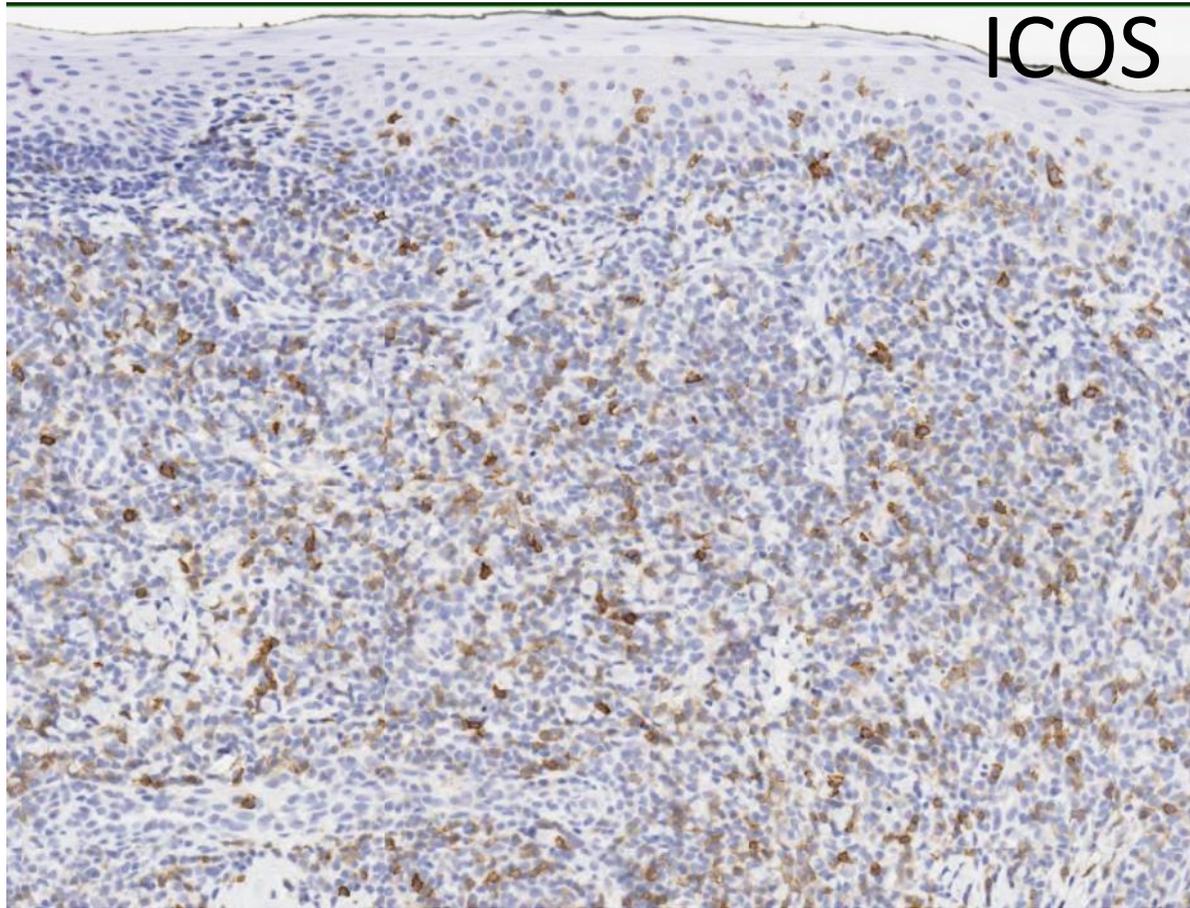
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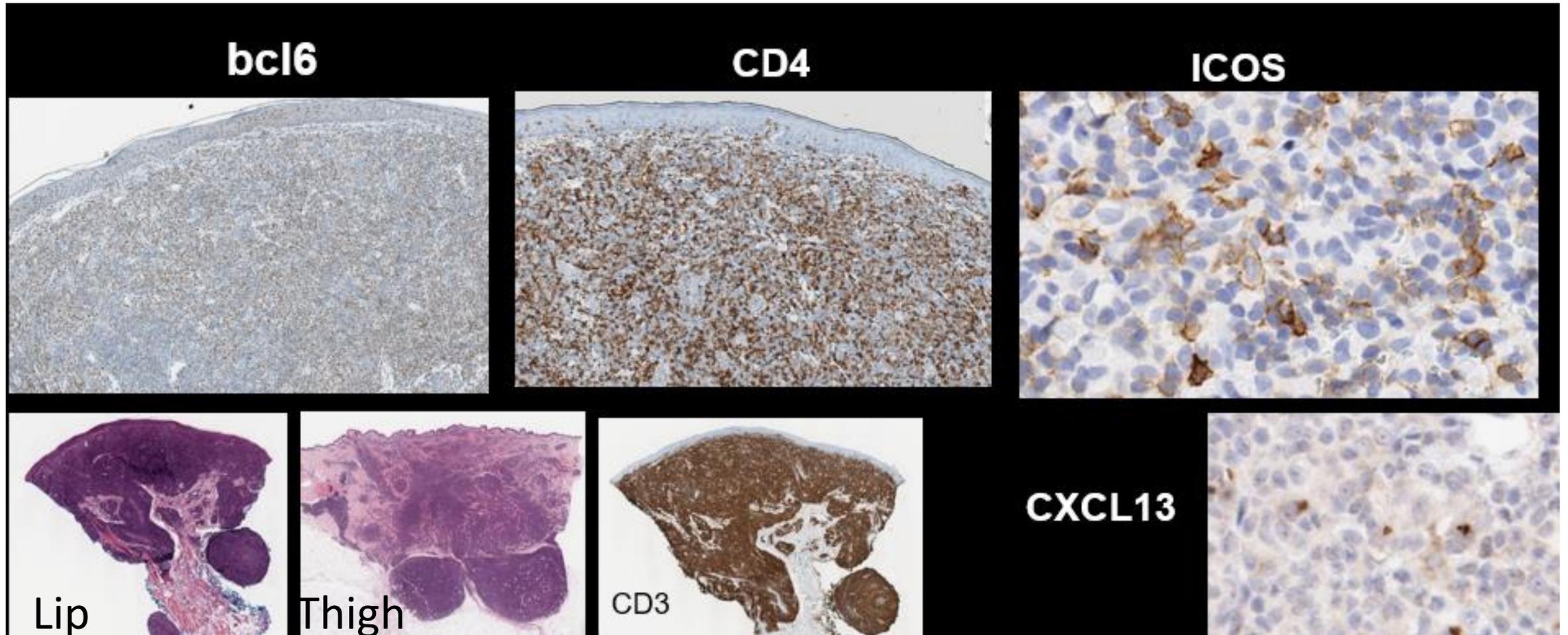


Vasculocentric



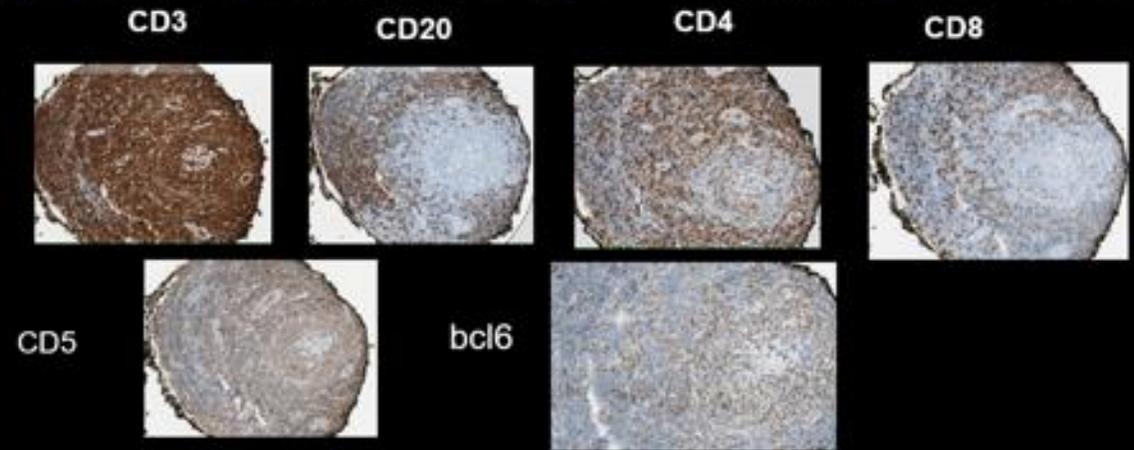
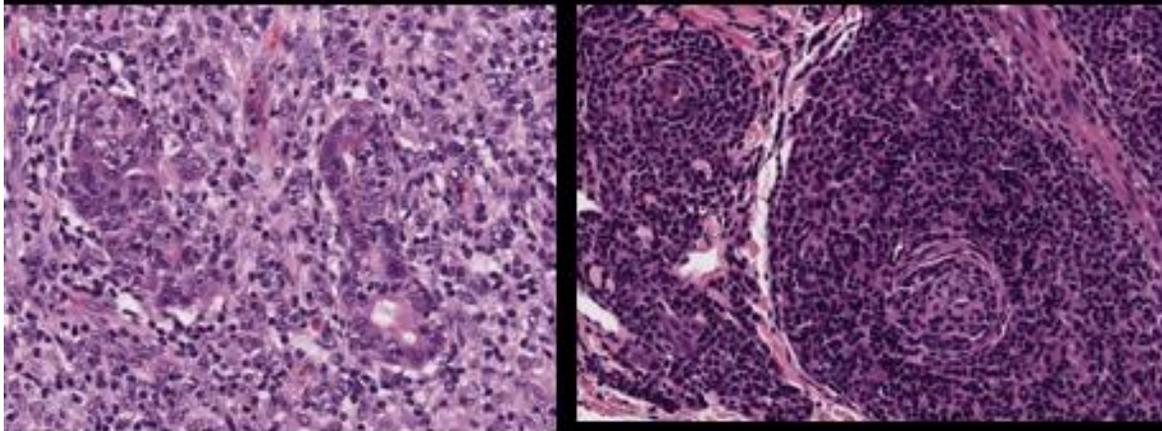
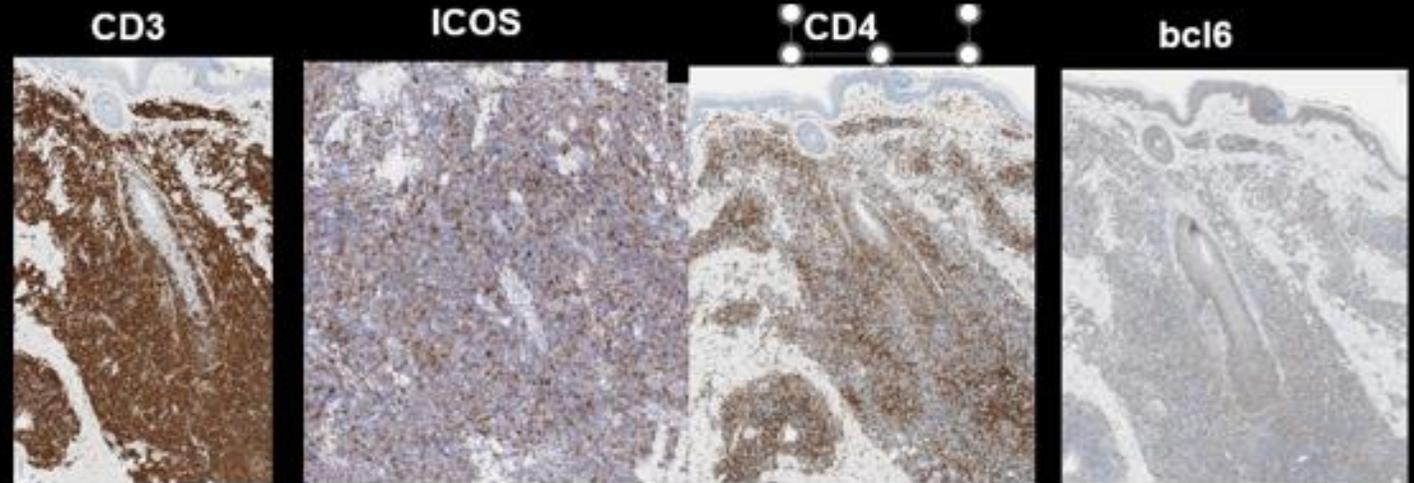
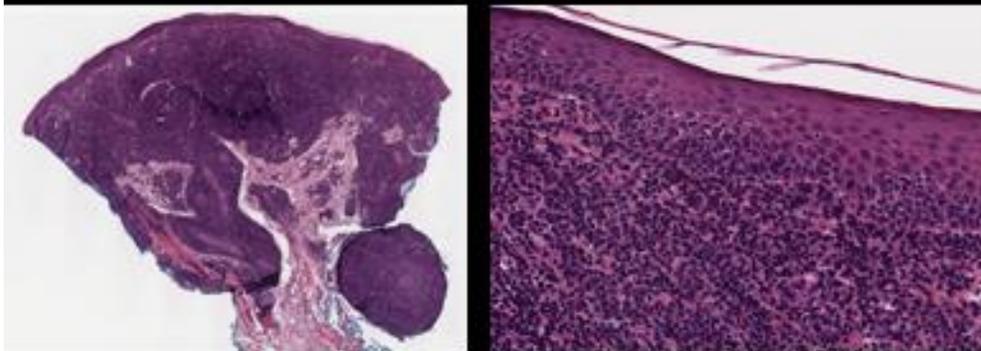


Lip lesion with same clone as thigh

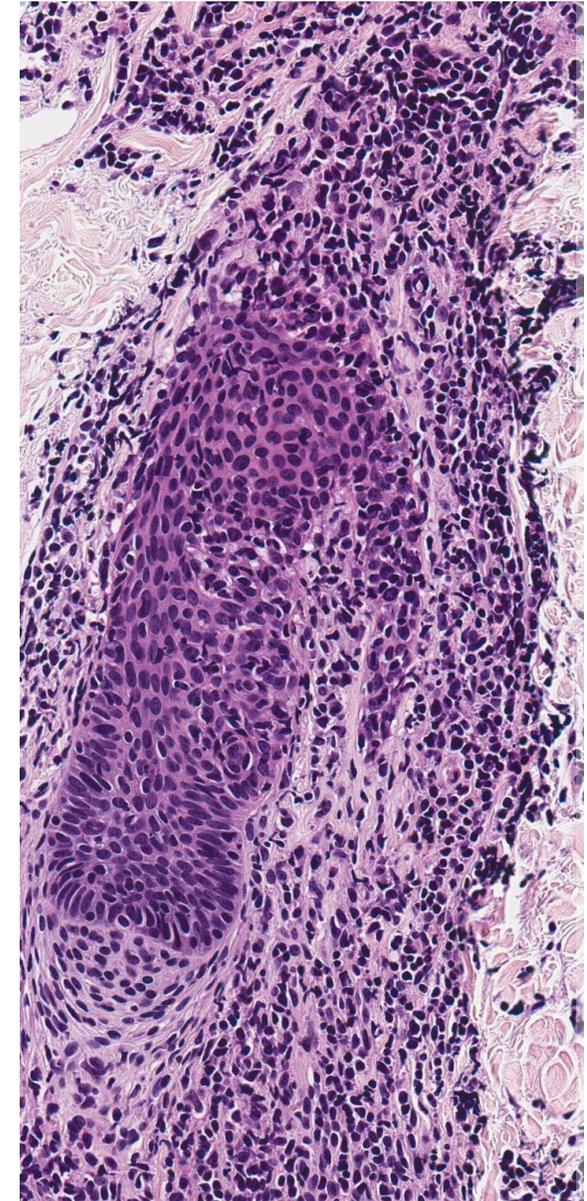
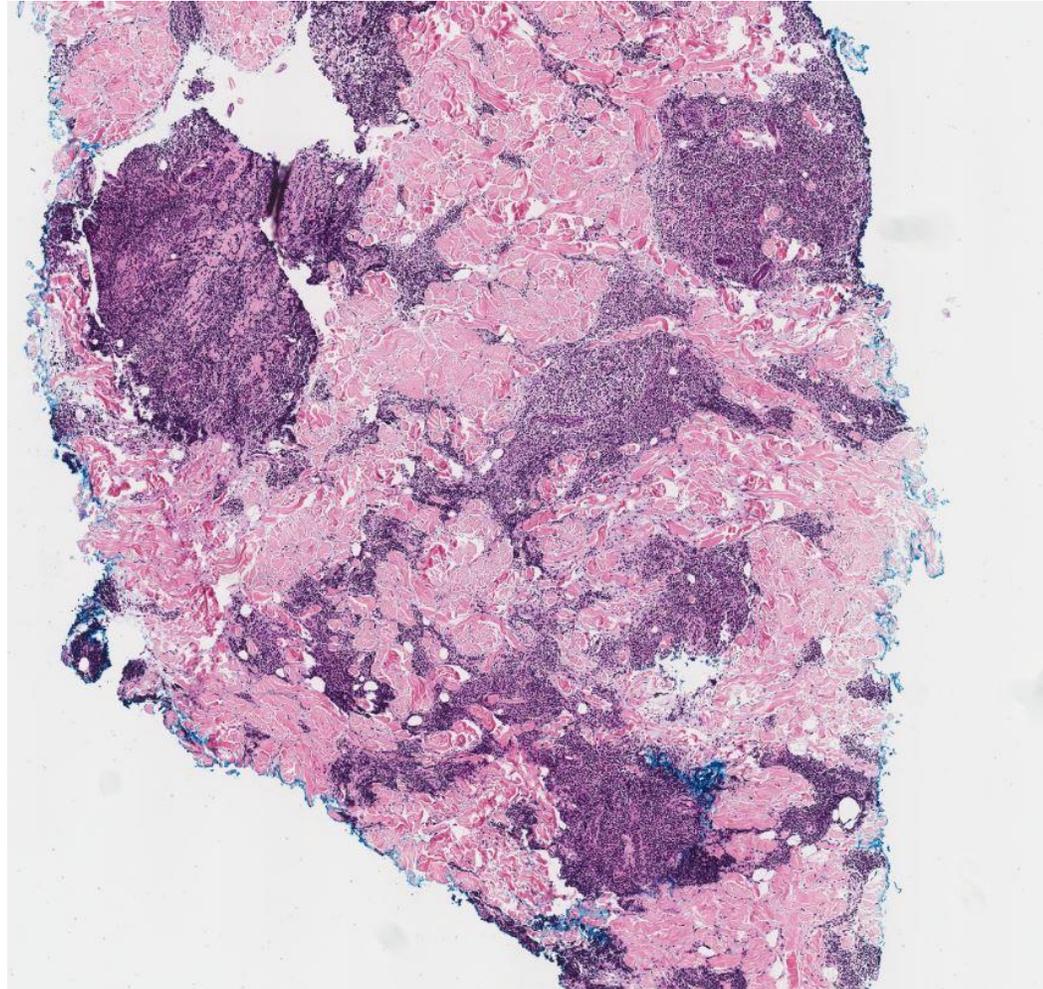
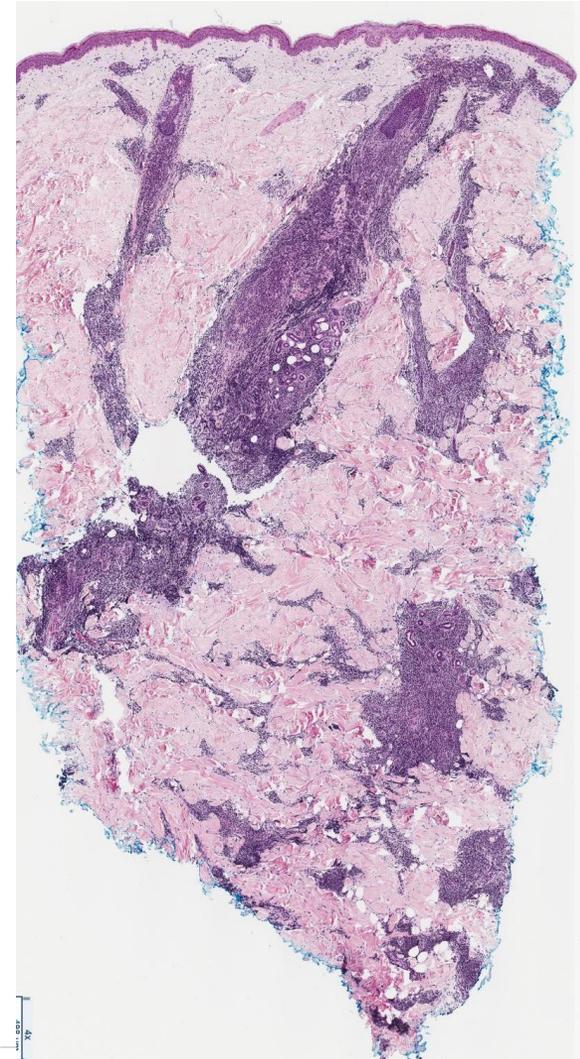


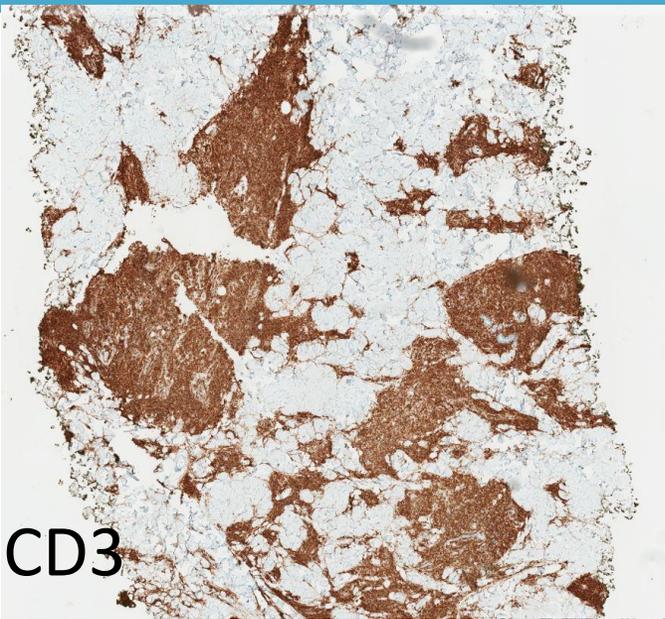
PCFHTCL with adnexotropism, vasculocentrism

XRT: no recurrence

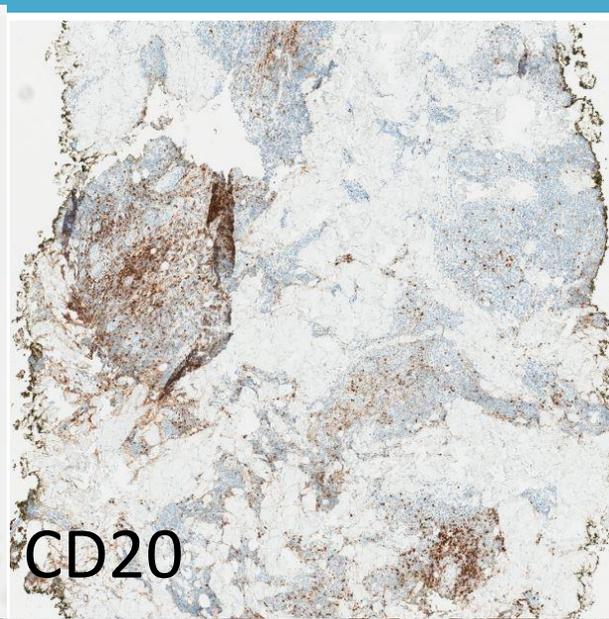


Nodule left shoulder: Incidental finding on routine 16 mon F/U

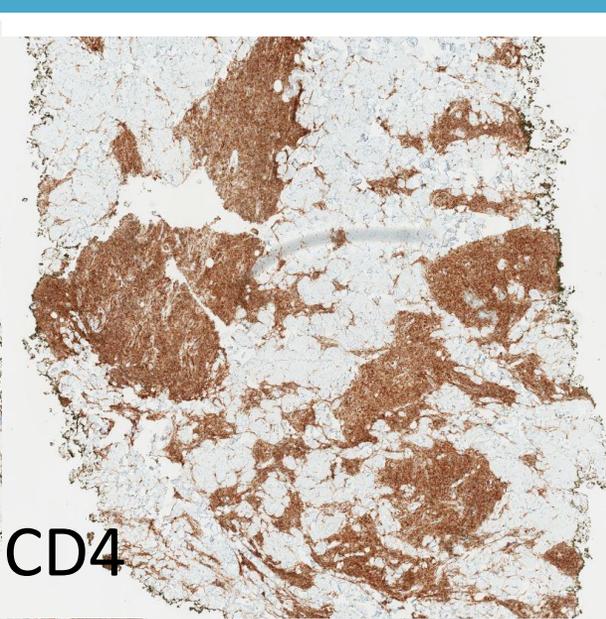




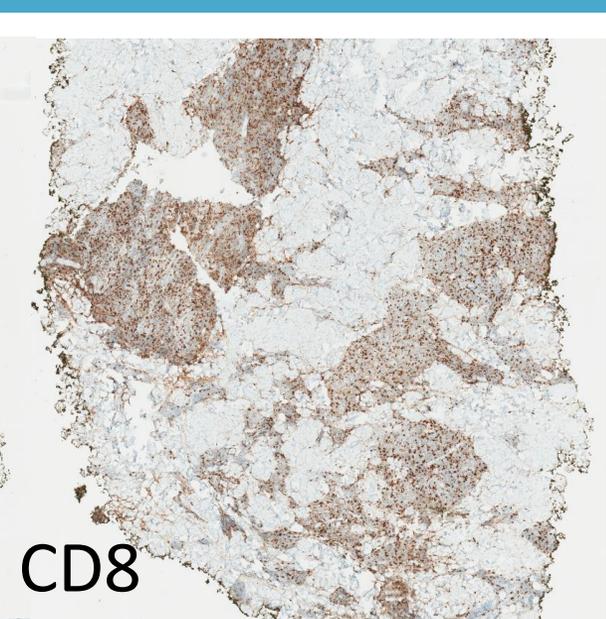
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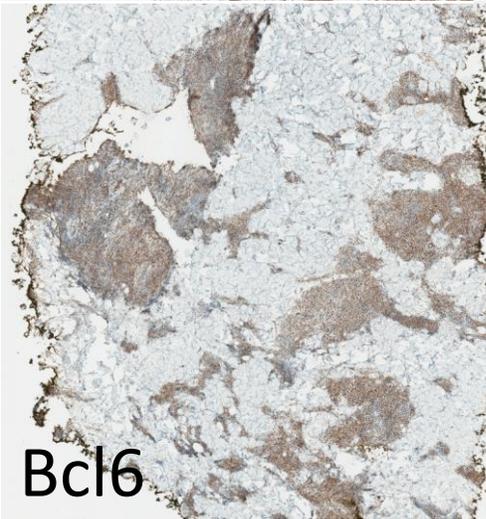
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CD4



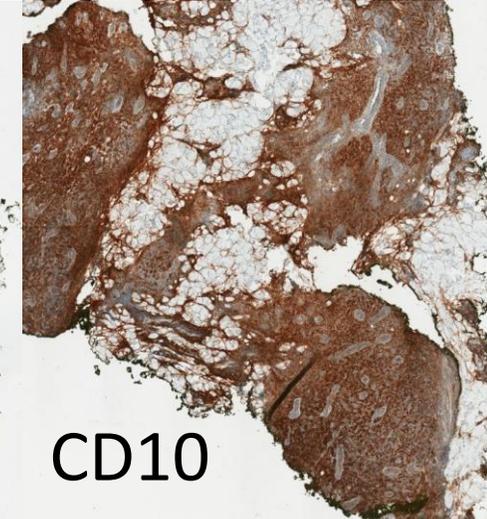
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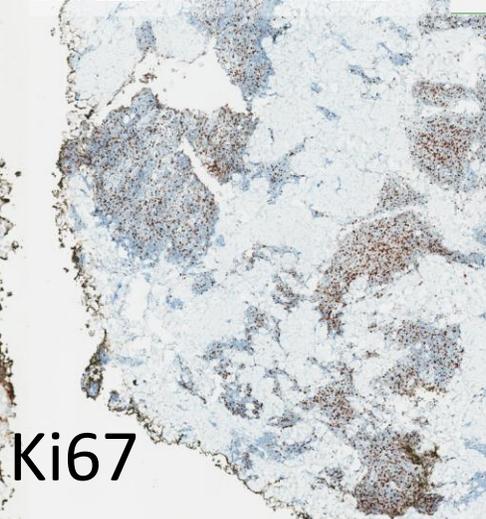
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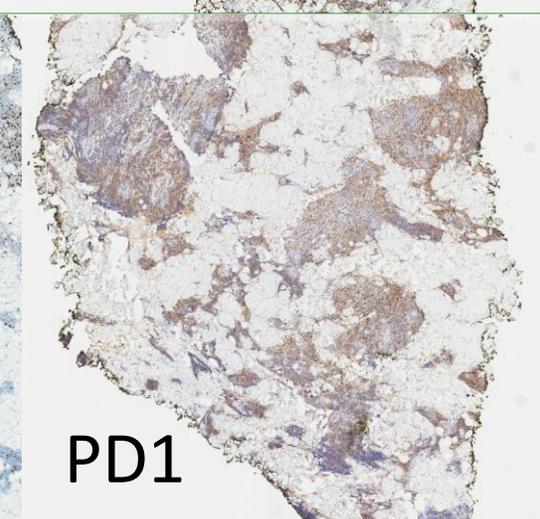
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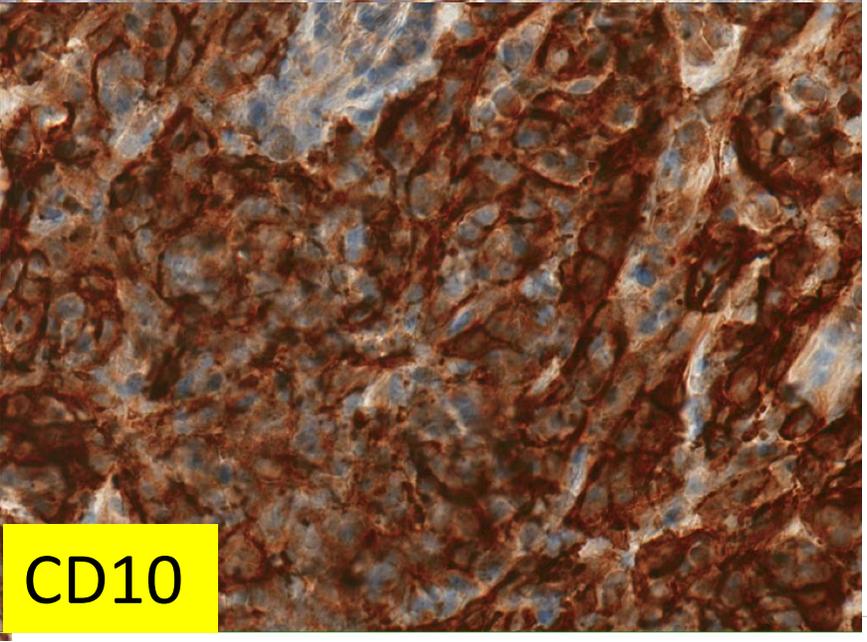
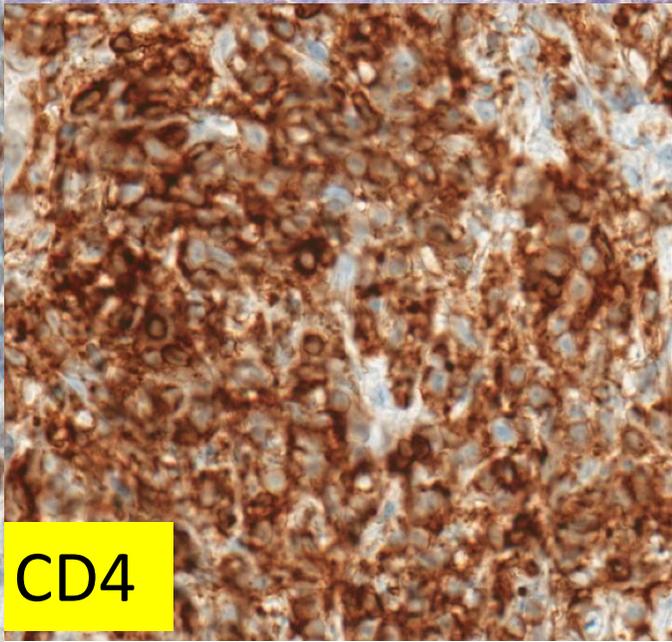
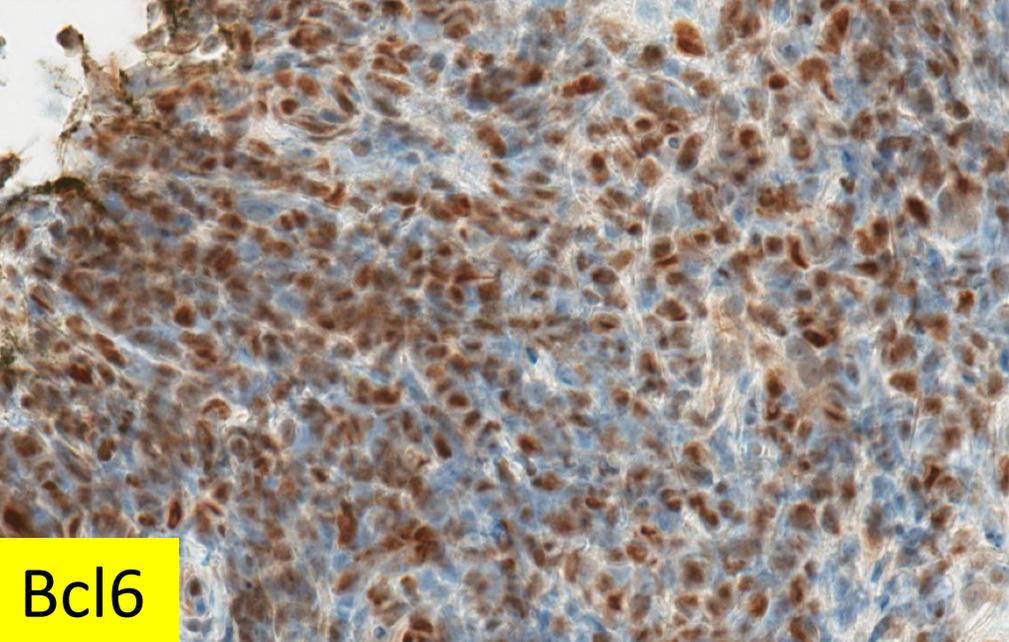
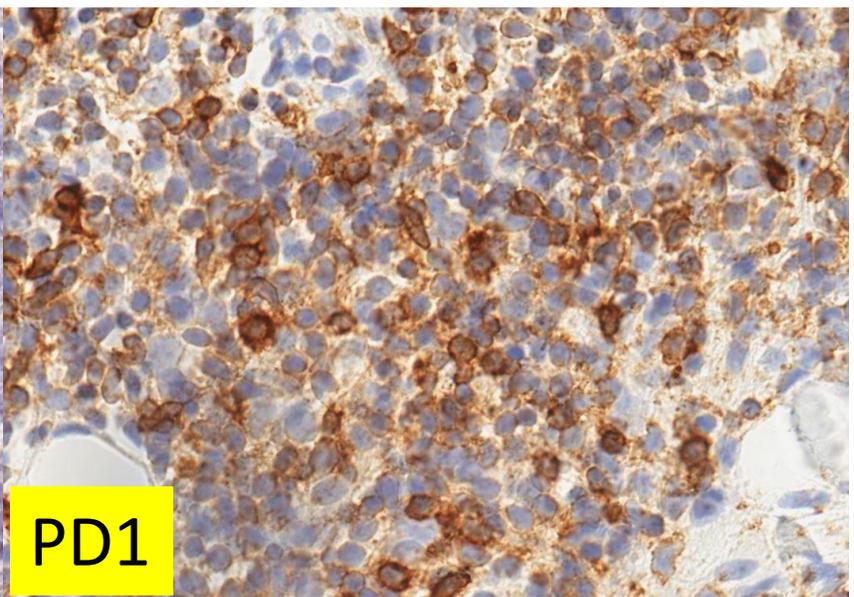
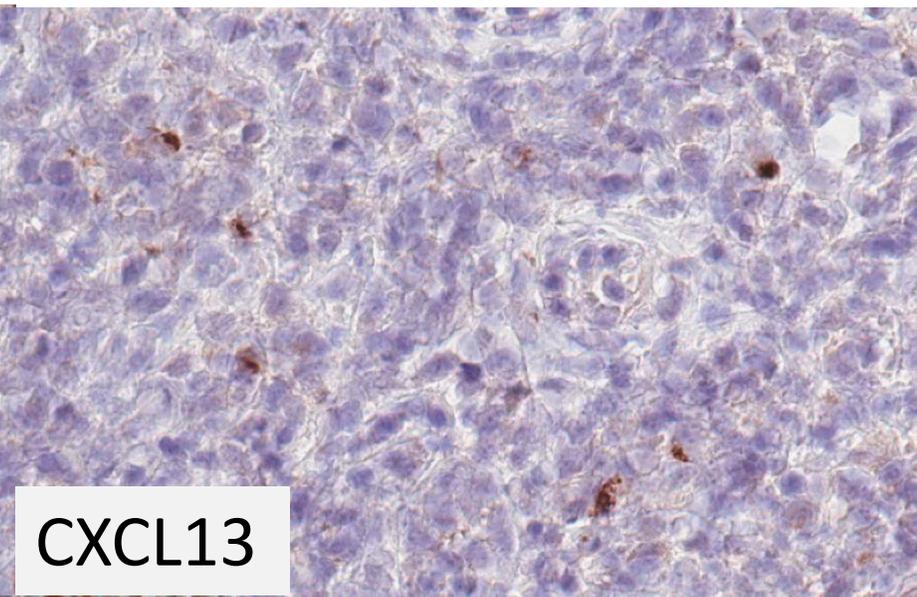
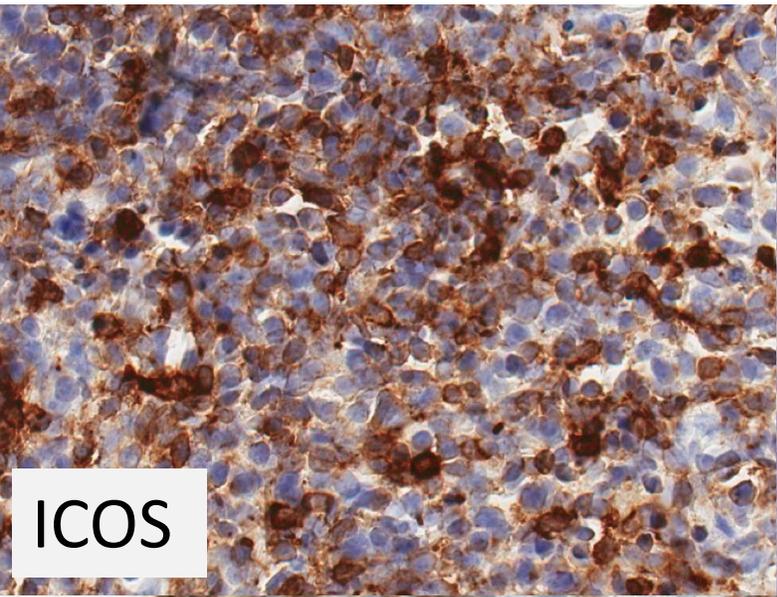
CD10



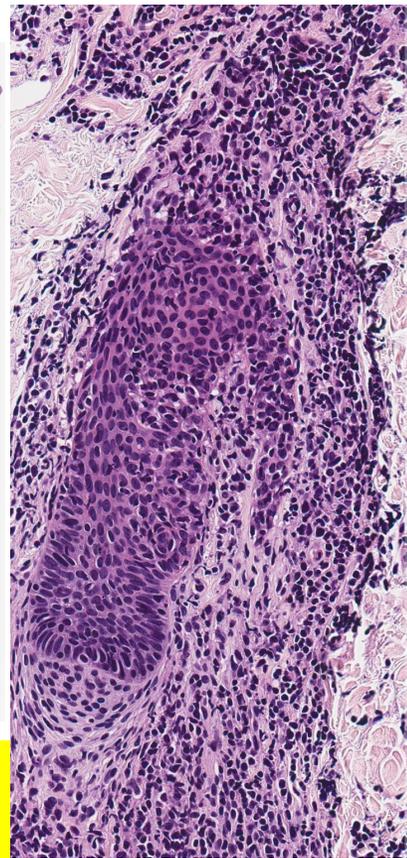
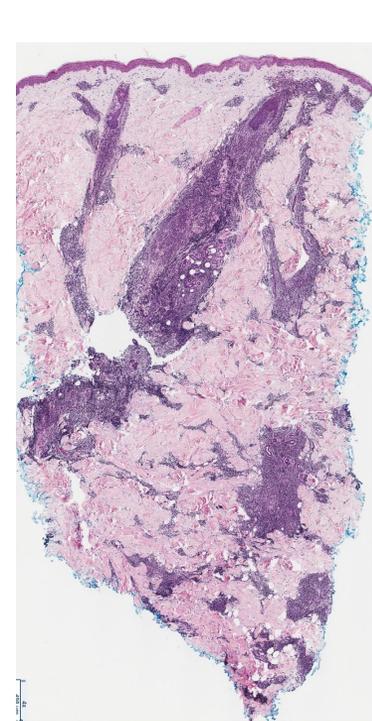
Ki67



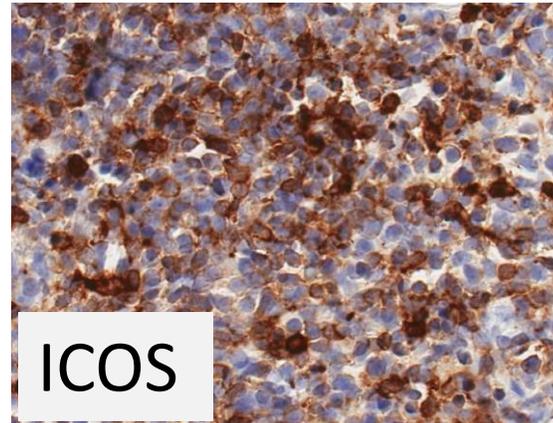
PD1



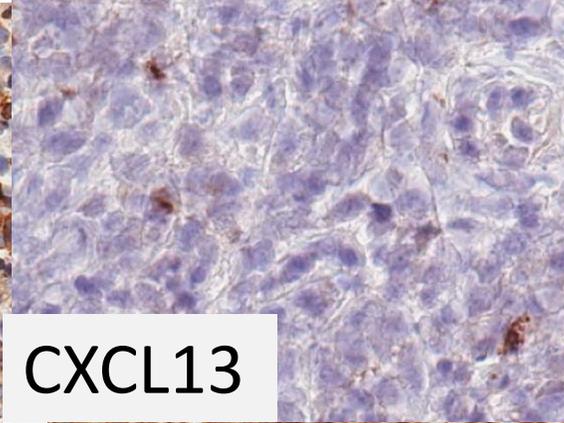
Primary cutaneous follicular helper T cell lymphoma



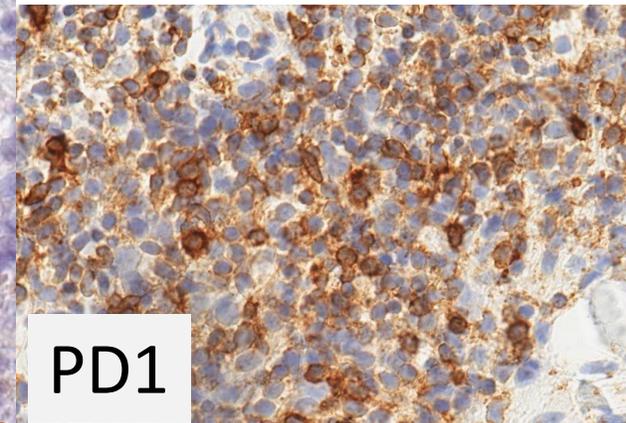
No recurrence
post Bx



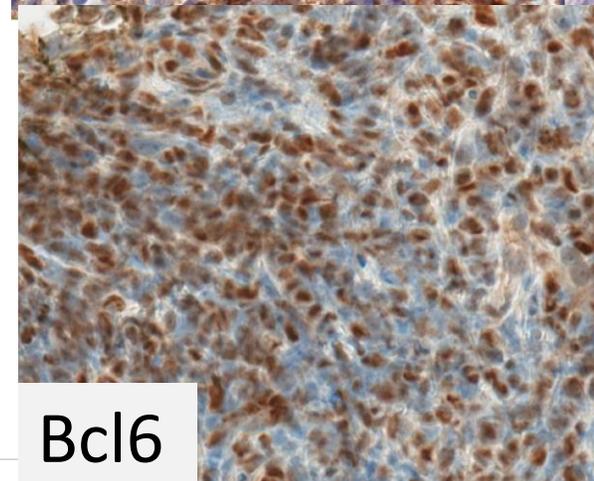
ICOS



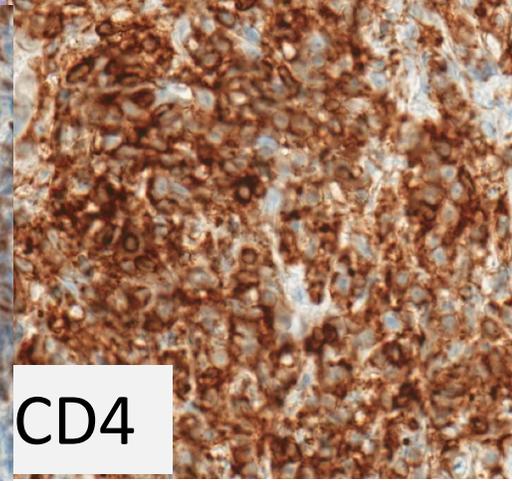
CXCL13



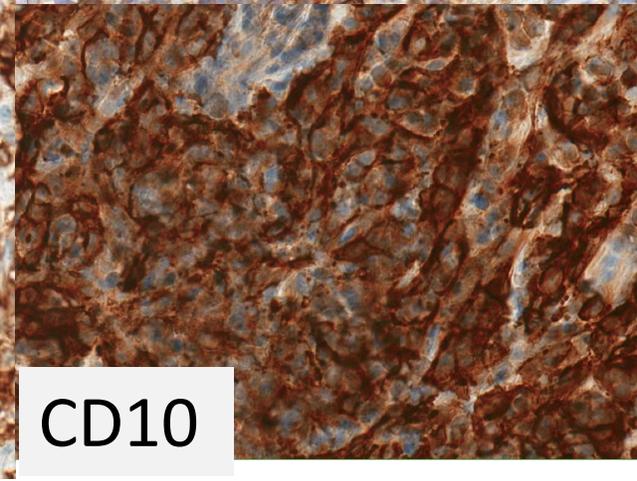
PD1



Bcl6

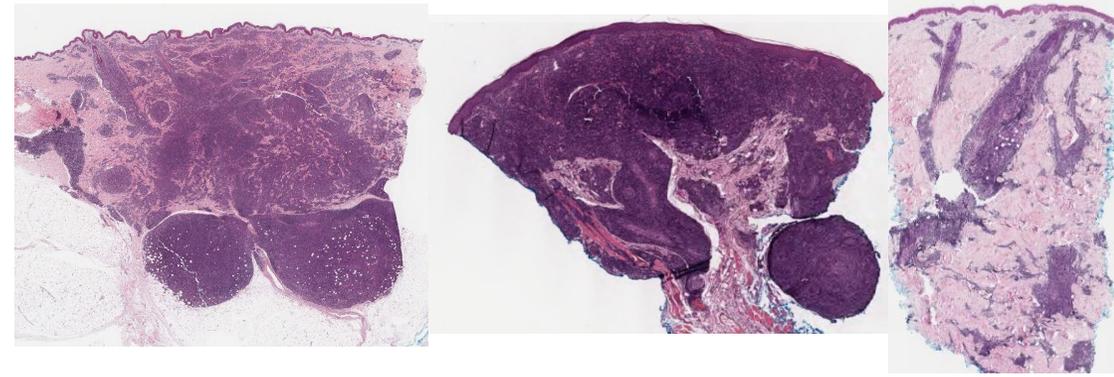


CD4



CD10

3 PTCL with TFH immunophenotype



Thigh, lip, shoulder: NED 3yr FU

Folliculotropism, syringotropism, angiocentricity (w/o angiodestruction)

(+): CD3, CD5, CD7, Bcl6, CD4 weak/partial (two tumors)

(+) Variable intensity of T_{FH} markers between tumors: CD4, PD1, ICOS, CD10

(+) Ki67, moderately elevated

(-) EBER

Peripheral lymphoma with T-follicular helper phenotype

- T-follicular helper (TFH) phenotype defined as at least 2 (3 preferred) TFH markers:
 - PD1, Bcl6, ICOS, CD10, CXCL13
- 3 WHO recognized lymphomas of T-follicular helper origin:
 - Angioimmunoblastic T-cell lymphoma (AITL), follicular T-cell lymphoma, other nodal peripheral T-cell lymphoma with a TFH phenotype
 - Similar genetic profiles: TET2, DNMT3A, RHOA mutations
 - All may secondarily involve skin
- Primary cutaneous CTCLs with TFH expression: PC CD4+ SMTLPD, MF/SS (PD1)
- Primary cutaneous peripheral TCL with TFH expression not well defined

BJD (2022) 187, pp970–980
Cancer, 2017; 585
Am J Surg Pathol 2017;
41:1581–92

Primary Cutaneous Follicular Helper T-cell Lymphoma

Arch Dermatol. 2012;148(7):832-839.

A New Subtype of Cutaneous T-cell Lymphoma Reported in a Series of 5 Cases

Maxime Battistella, MD; Marie Beylot-Barry, MD, PhD; Hervé Bachelez, MD, PhD; Jacqueline Rivet, MD, PhD; Béatrice Vergier, MD, PhD; Martine Bagot, MD, PhD

Primary Cutaneous Follicular Helper T-Cell Lymphoma: A Case Series and Review of the Literature

Am J Dermatopathol 2017;39:374–383

James Y. Wang, MD,* Giang Huong Nguyen, MD, DPhil,†
Jia Ruan, MD, PhD,‡ and Cynthia M. Magro, MD*

Primary cutaneous peripheral T-cell lymphomas with a T-follicular helper phenotype: an integrative clinical, pathological and molecular case series study*

Luojun Wang ^{1,2} Delphine Rocas,³ Stéphane Dalle,⁴ Nouhoum Sako,² Laura Pelletier,² Nadine Martin,² Aurélie Dupuy,² Nadia Tazi,¹ Brigitte Balme,³ Béatrice Vergier,^{5,6} Marie Beylot-Barry ^{6,7} Agnès Carlotti,⁸ Martine Bagot ⁹ Maxime Battistella,¹⁰ Guillaume Chaby ¹¹ Saskia Ingen-Housz-Oro ¹² Philippe Gaulard^{1,2} and Nicolas Ortonne ^{1,2}

British Journal of Dermatology (2022) 187, pp970–980

Primary Cutaneous Follicular Helper T-cell Lymphoma: Clinical

- Adults mean and median age mid 60's (22-95 yrs)
- Nodules> papules>>plaques: multiple> >solitary
- T3b> T3a, T1-T2
- Trunk, upper and lower limbs> face/head/scalp
- LDH mostly normal (rare increased)
- Often resistant to CTCL treatment (early recurrences), requiring chemotherapy; XRT if localized
- Indolent> rare extracutaneous spread and death



Battistella M et al. Arch Derm. 2012;148(7):832-839

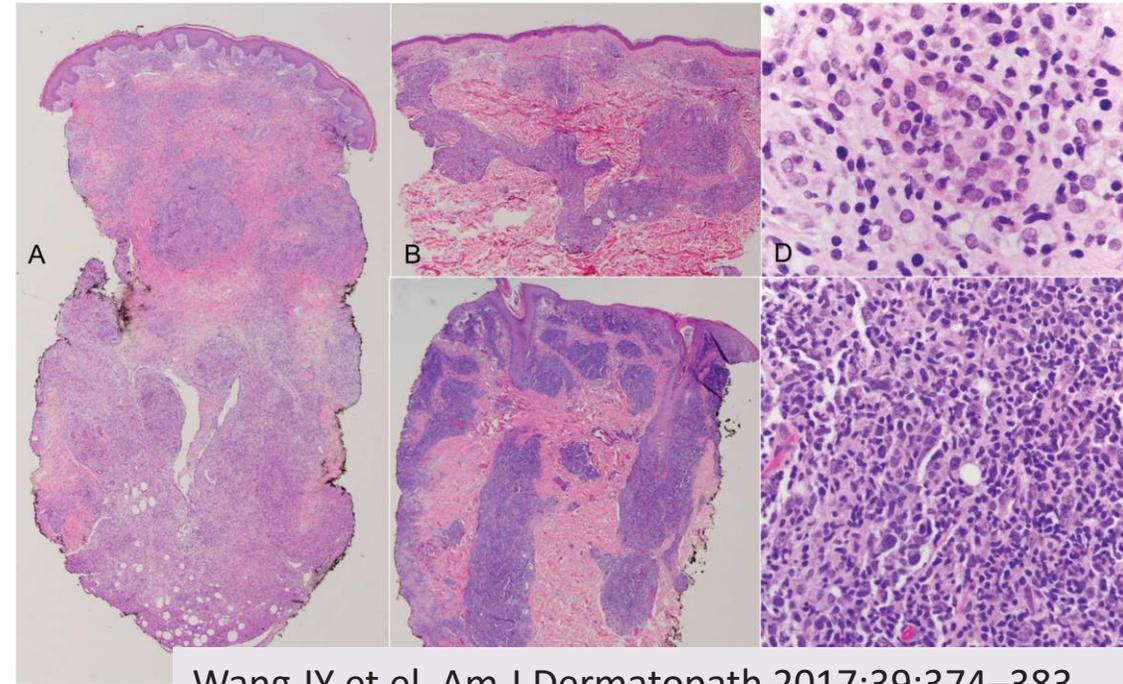
Arch Dermatol. 2012;148(7):832-839

Am J Dermatopathol 2017;39:374-383

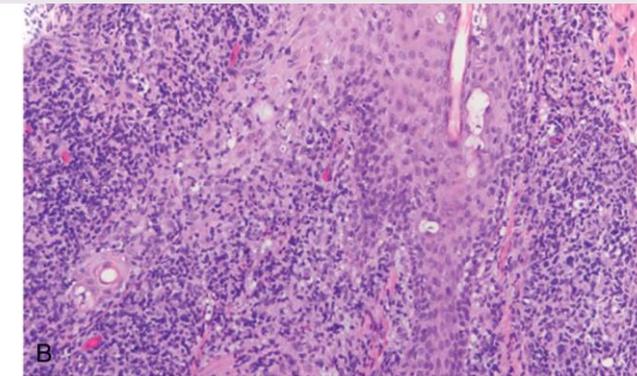
British Journal of Dermatology (2022) 187, pp970-980.

Primary Cutaneous Follicular Helper T-cell Lymphoma: Histology

- Nodular dermal, deep dermis, subcutaneous, without epidermotropism
- Medium-large cells > small/medium cells (not cerebriform)
- Syringotropism, folliculotropism, angiocentricity reported
- Rare granulomatous component, rare eosinophils



Wang JY et al. Am J Dermatopath 2017;39:374–383



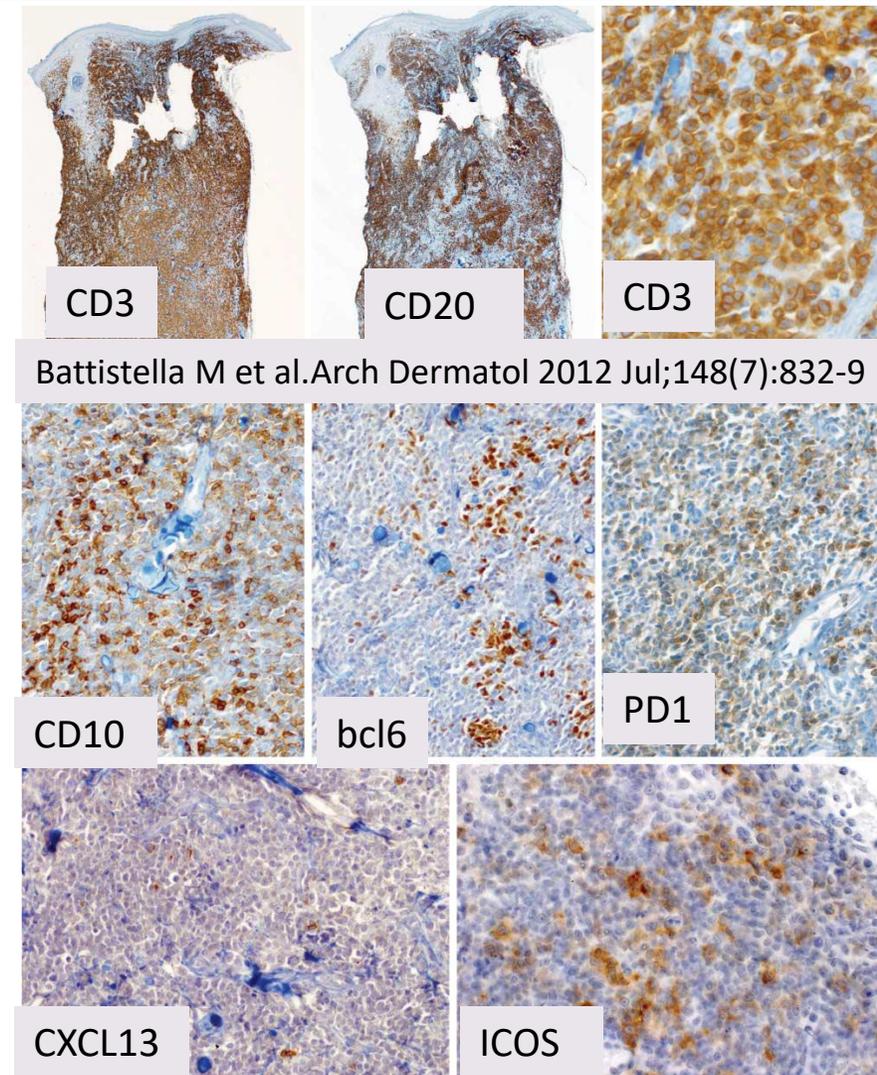
Arch Dermatol. 2012;148(7):832-839

Am J Dermatopathol 2017;39:374–383

British Journal of Dermatology (2022) 187, pp970–980.

Primary Cutaneous Follicular Helper T-cell Lymphoma: Immunophenotype

- TFH markers variable between tumors:
 - Most frequent PD-1 and, ICOS
 - Bcl6 and CD10 (+) or (-)
 - CXCL13 scattered to sparse
 - Case report of negative PD1 with recurrent tumor
- B-cell component often prominent:
 - May see B-cell clone
 - Bcl6 expression often led to erroneous PCFCL diagnosis
- Ki67 moderately high (30-50%)
- (+) T cell clone: skin, blood (if widespread) +/- marrow;



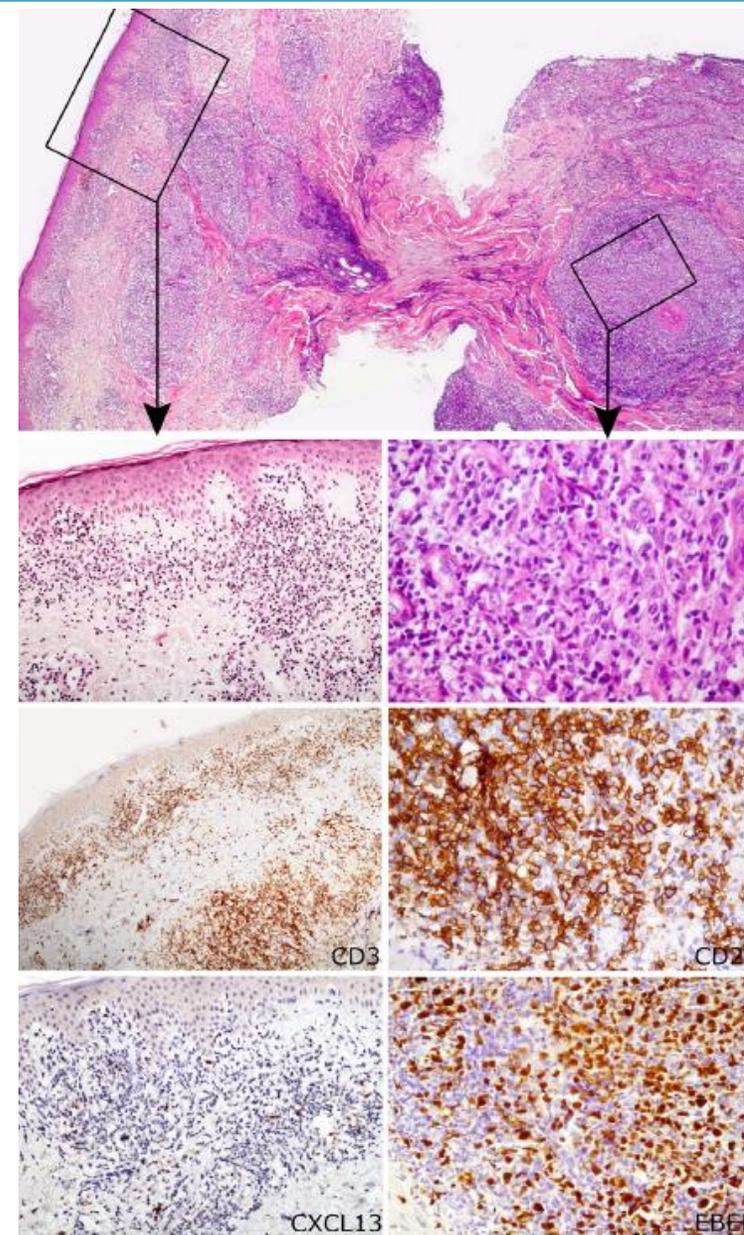
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J Cutan Pathol 2013; 40:903-8

Primary cutaneous peripheral T-cell lymphomas with a T-follicular helper phenotype: an integrative clinical, pathological and molecular case series study*

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- 23 pts with peripheral T cell lymphoma with TFH phenotype: characterized clinical, path and molecular features
- 10 of 23 patients: EBV+ B cells, clonal expansion of B or plasma cells, and/or accompanying neoplastic B-cell proliferation
 - 5/10 without aggressive disease
- Three (13%) developed systemic disease and died of lymphoma. Nine (39%) received >1 line of chemotherapy
- Overall survival of 78% (at 98 months): no demographic associations



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- Targeted next-generation sequencing revealed genetic alterations:
 - Mutated TET2, RHOA G17V (similar to AITL/ systemic TFH-PTCL), TET2/DNMT3A/PLCG1/SETD2 mutational profile, isolated mutations (TET2, PLCG1, SETD, STAT5B)
- 4 cases with AITL-like mutational profile (TET2, RHOA):
 - TET2 RHOA mutational profile was not indicative of aggressive behavior or survival
 - It was strongly associated with the presence of a clonal B-cell population

Summary and Questions

- 3 examples of PC T-cell lymphoma with prominent bcl6 expression by T-cells:
 - clue to TFH immunophenotype
- Weak CD4:
 - Still diagnostic of primary cutaneous follicular helper T-cell lymphoma/PTCL with TFH phenotype?
- Prominent folliculotropism/syngotropism:
 - Consider this a histopathologic feature of PCFHTCL?
- Variable expression of TFH markers between tumors: CD10 (-), CD10 +, PD1 weak, PD1 strong
- Need for next generation sequencing?



Thank you!

