

Case 1

Michelly Sampaio
Hematopathology – NIH- CC – DLM
02/25/2026



National Institutes of Health
Clinical Center

Clinical Information

- 63-year-old male presenting with progressive fatigue, reduced appetite, and unintentional weight loss (at least 35 pounds) over the last two years.

WBC	3.05 K/mcL
Hgb	8.4 g/dL
HCT	24.7%
MCV	112.3 fL
PLT	38 K/mcL
ANC	2.23 K/mcL
ALC	0.67 K/mcL
AMoC	0.03 K/mcL

Relevant Past Medical History

- Hypertension
- Diabetes Mellitus, type 2
- Coronary Artery Disease
- Chondritis
- Inflammatory dermatoses

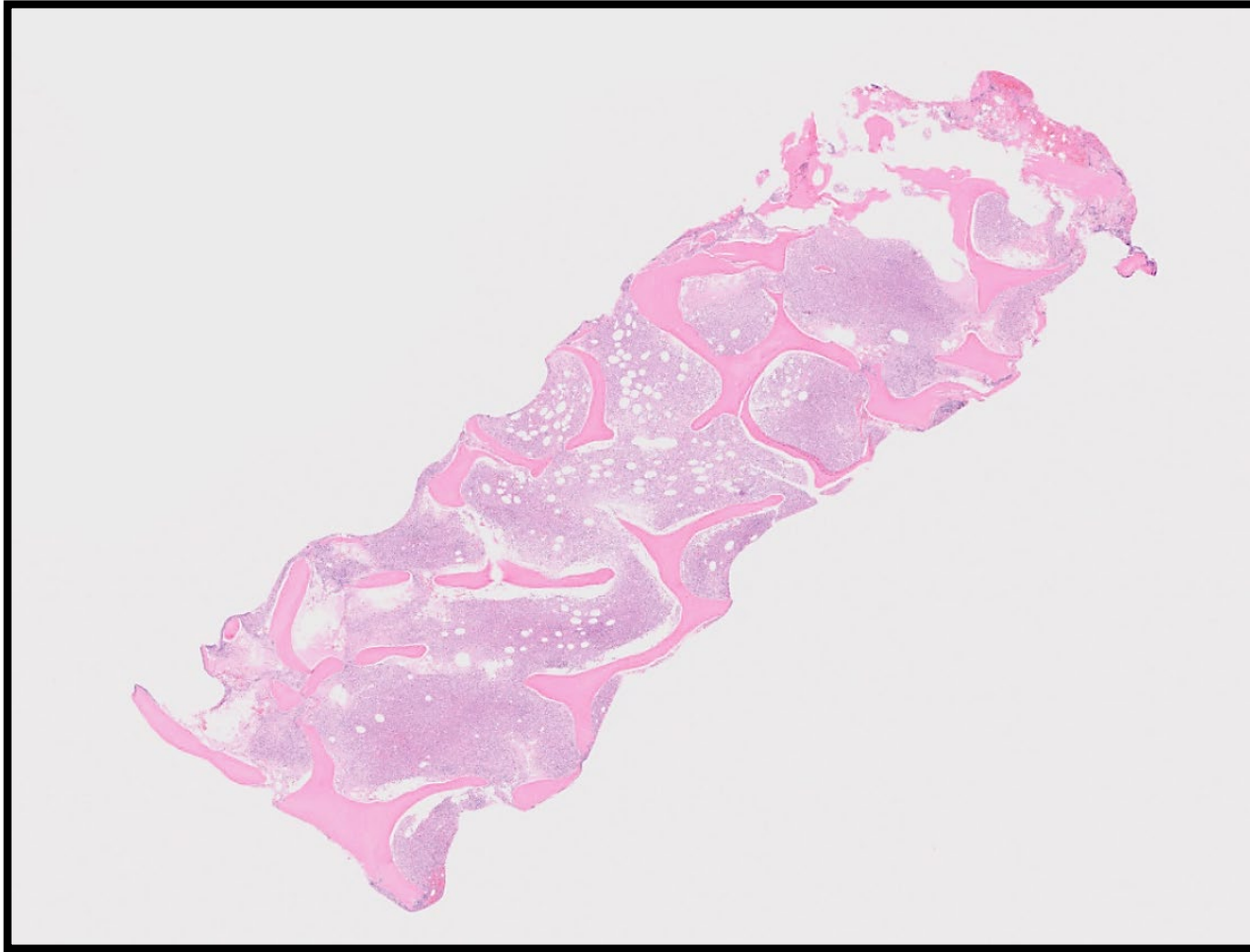
Additional Laboratory Investigation

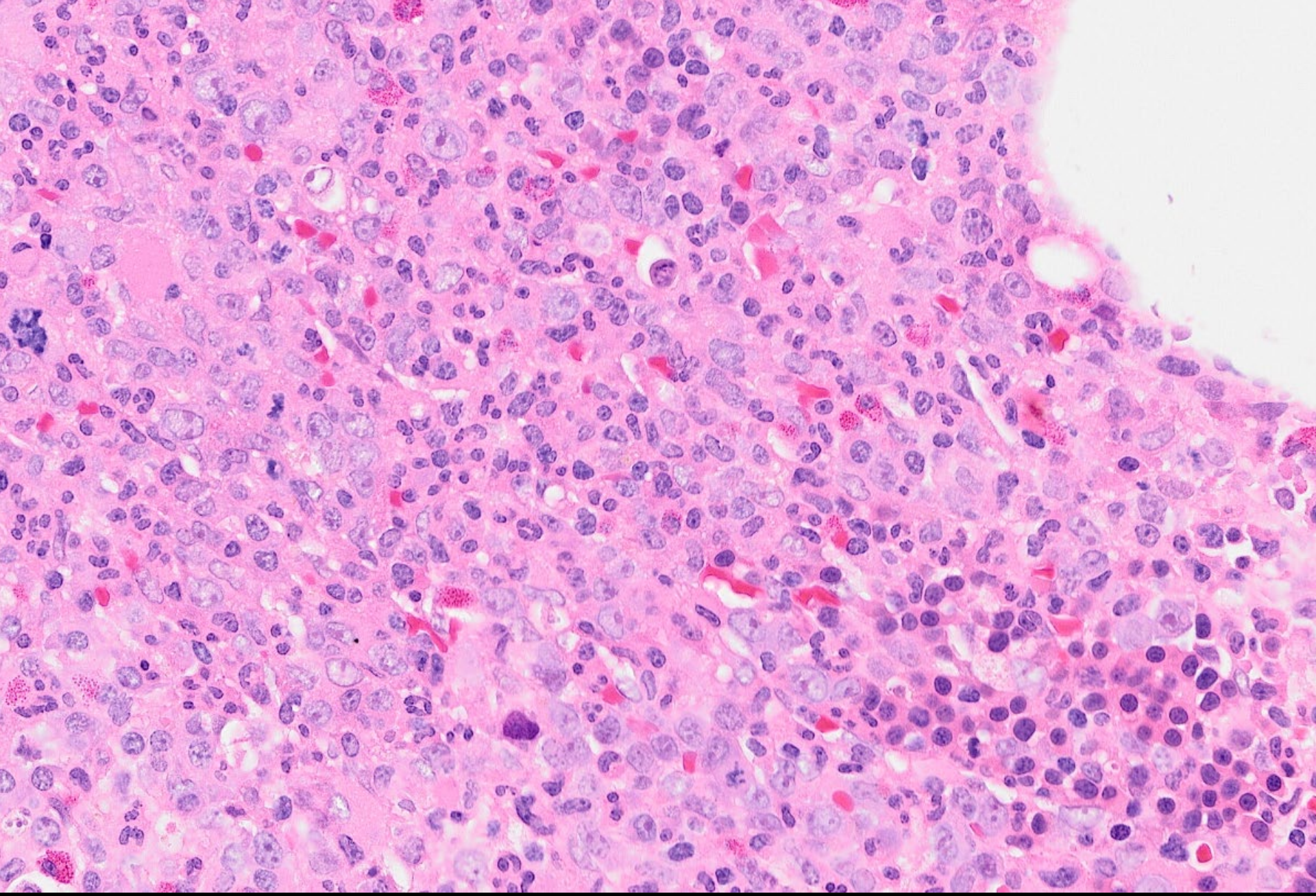
CRP	37.9mg/L
ESR	> 140
D-dimer	0.91
LDH	201
IgG	613
IgA	1212
IgM	66



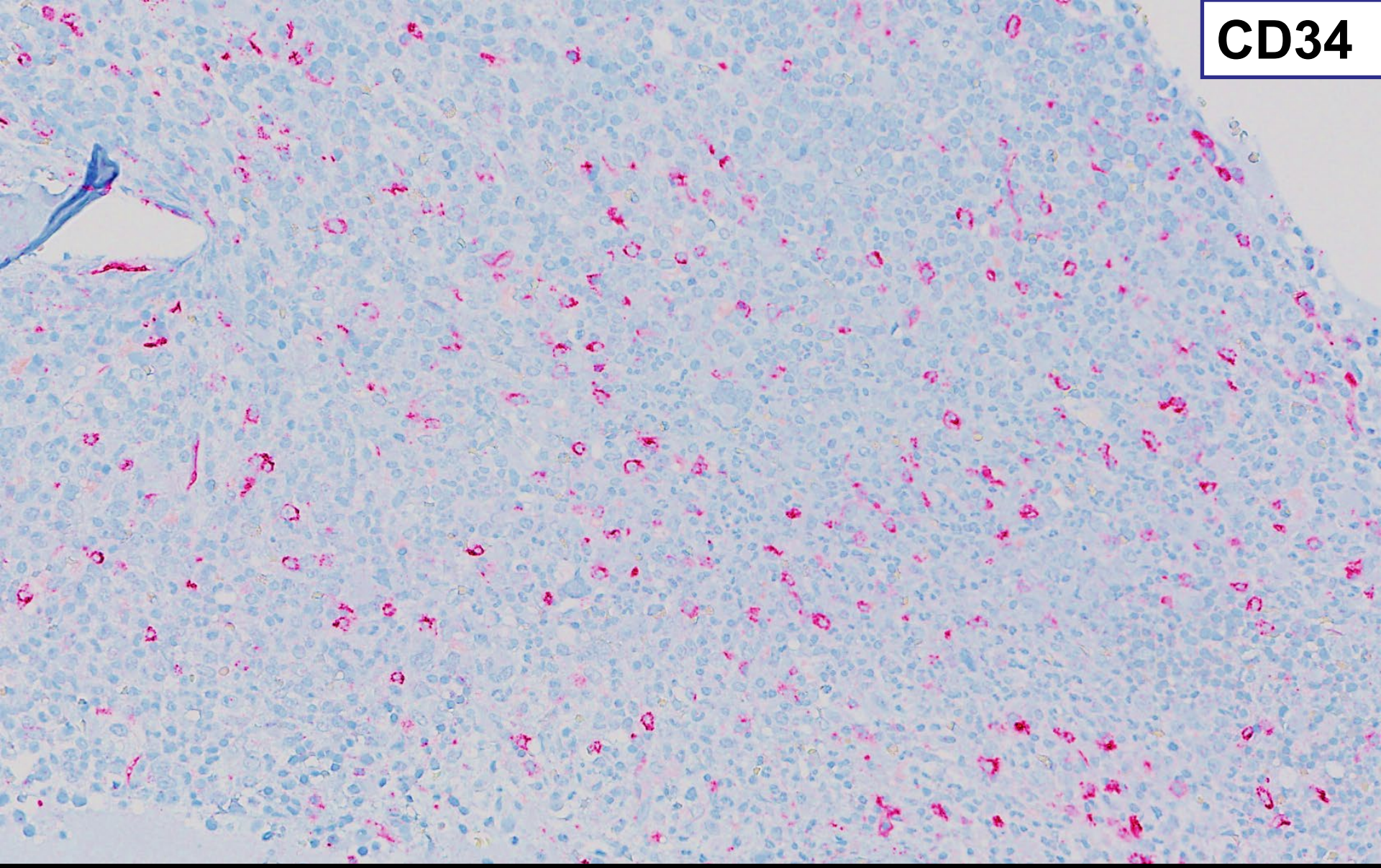
- Cytokine panel notable for:
 - Elevated TNF, IL-18, IL-6, IL-10 levels
- **IgA lambda** monoclonal protein by immunofixation
- M-spike: 0.3 g/dL
- Kappa/Lambda ratio: 0.1
 - Free kappa: 1.41 (0.33 – 1.94mg/dL)
 - Free lambda: 13.99 (0.57-2.63mg/dL)

Bone Marrow Biopsy



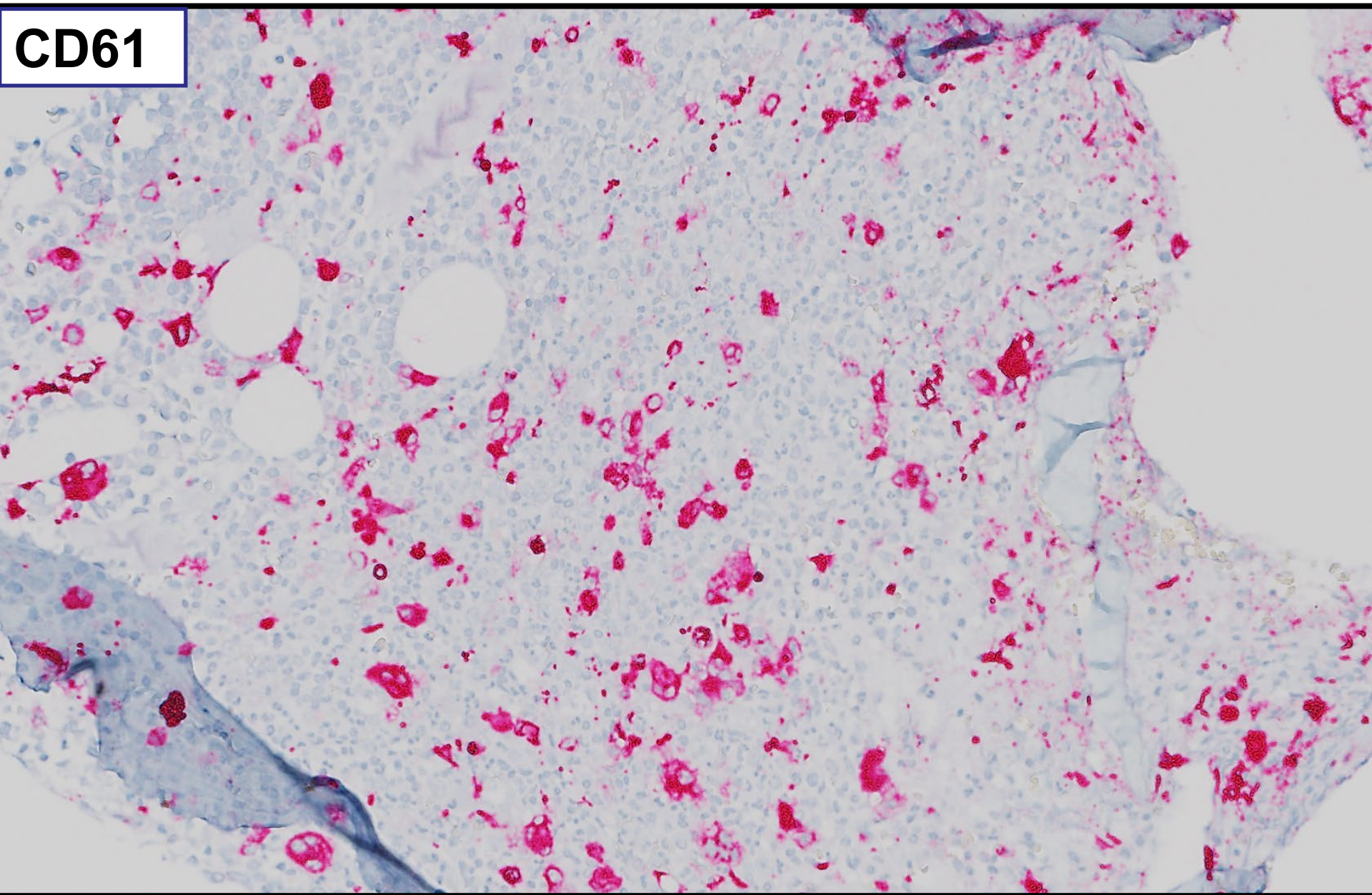






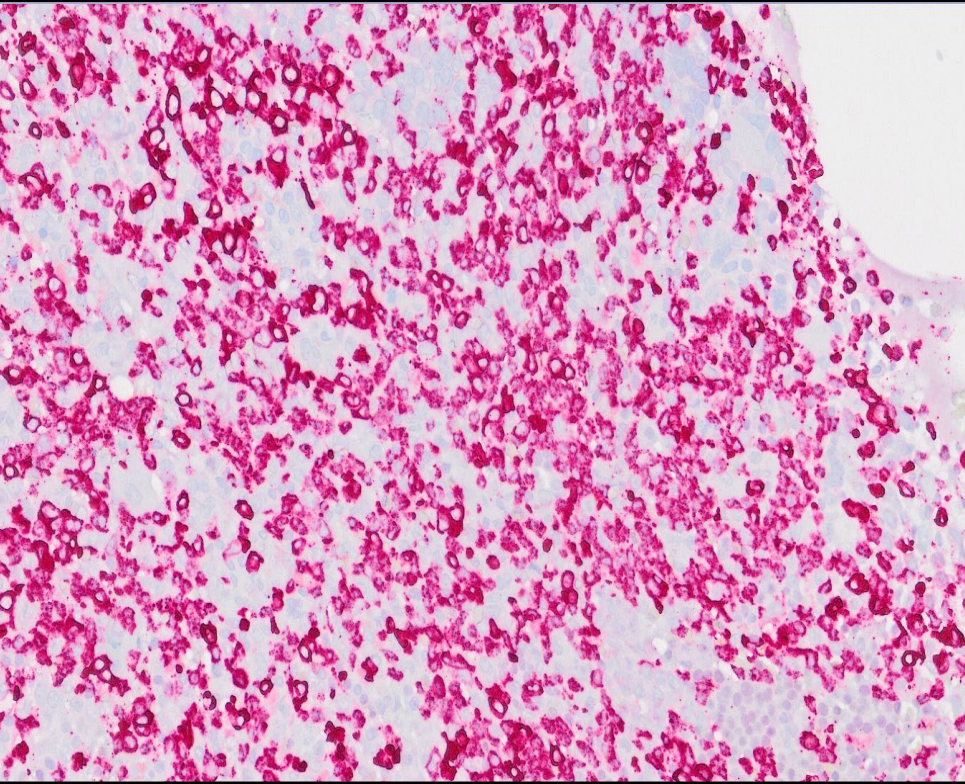
Increased (about 7-9%)

CD61

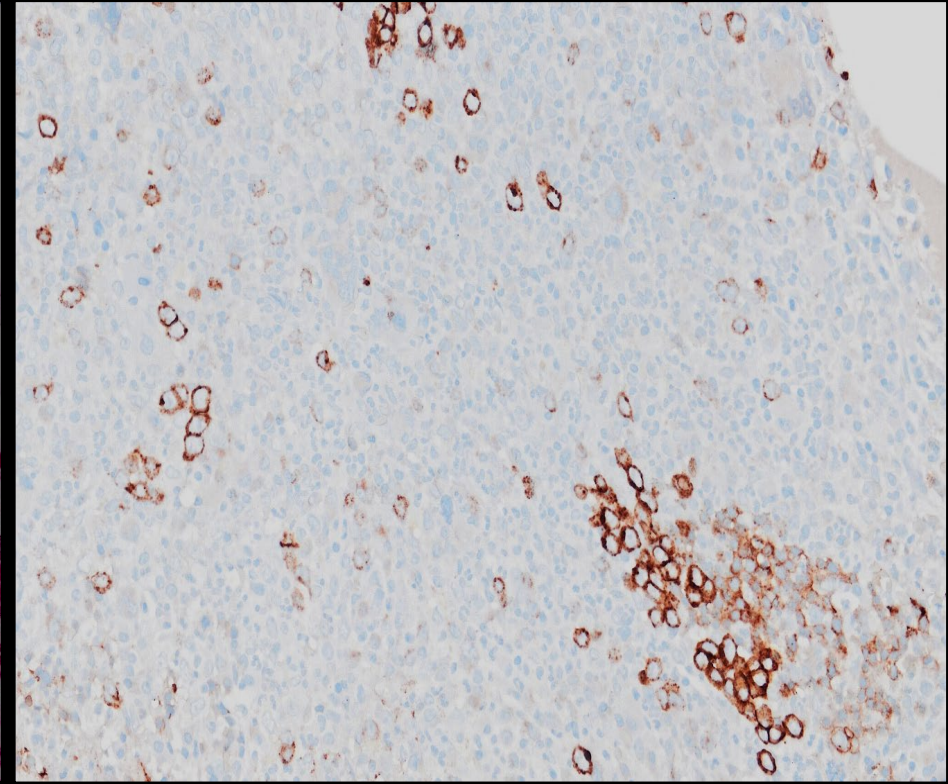


Increased number of plasma cells (20-30%) – atypical CD56 expression

MPO

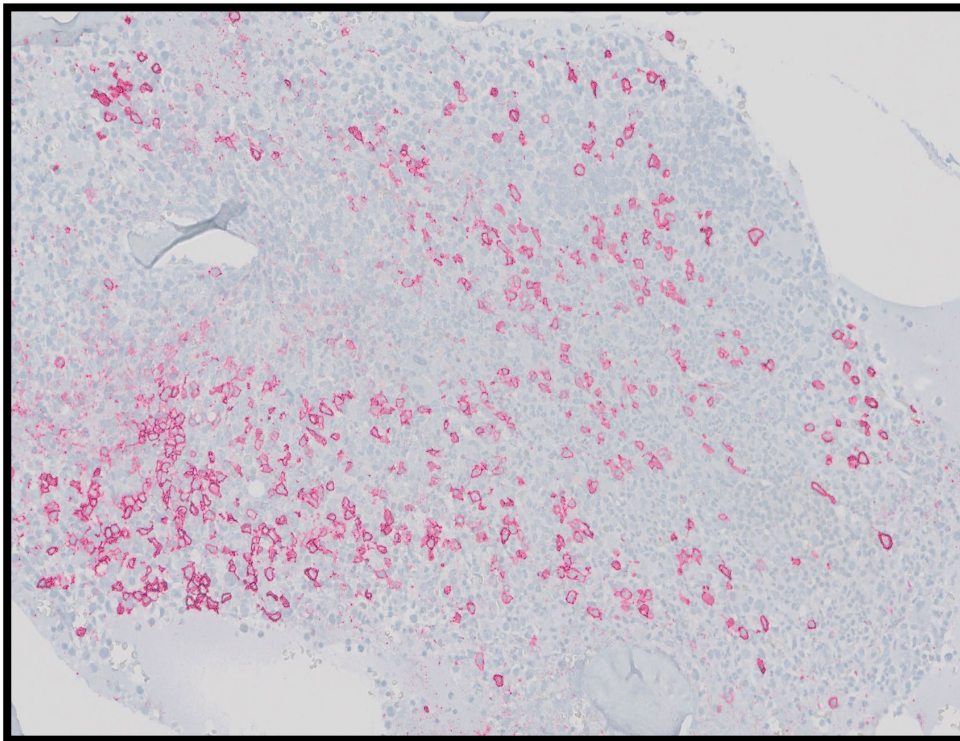


CD71

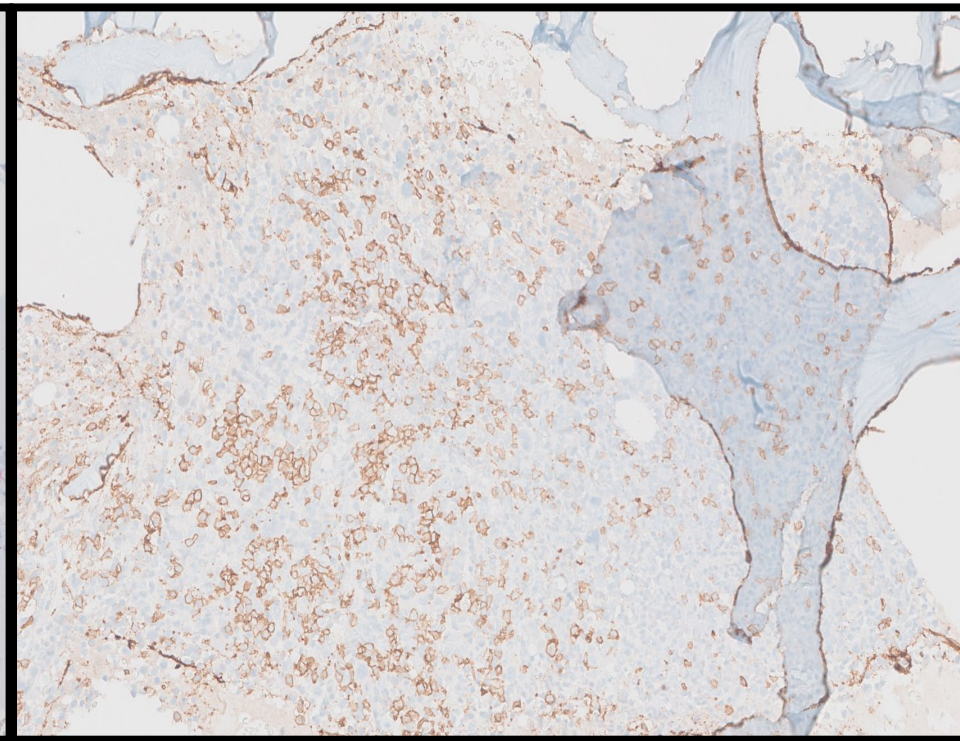


Increased number of plasma cells (20-30%) – atypical CD56 expression

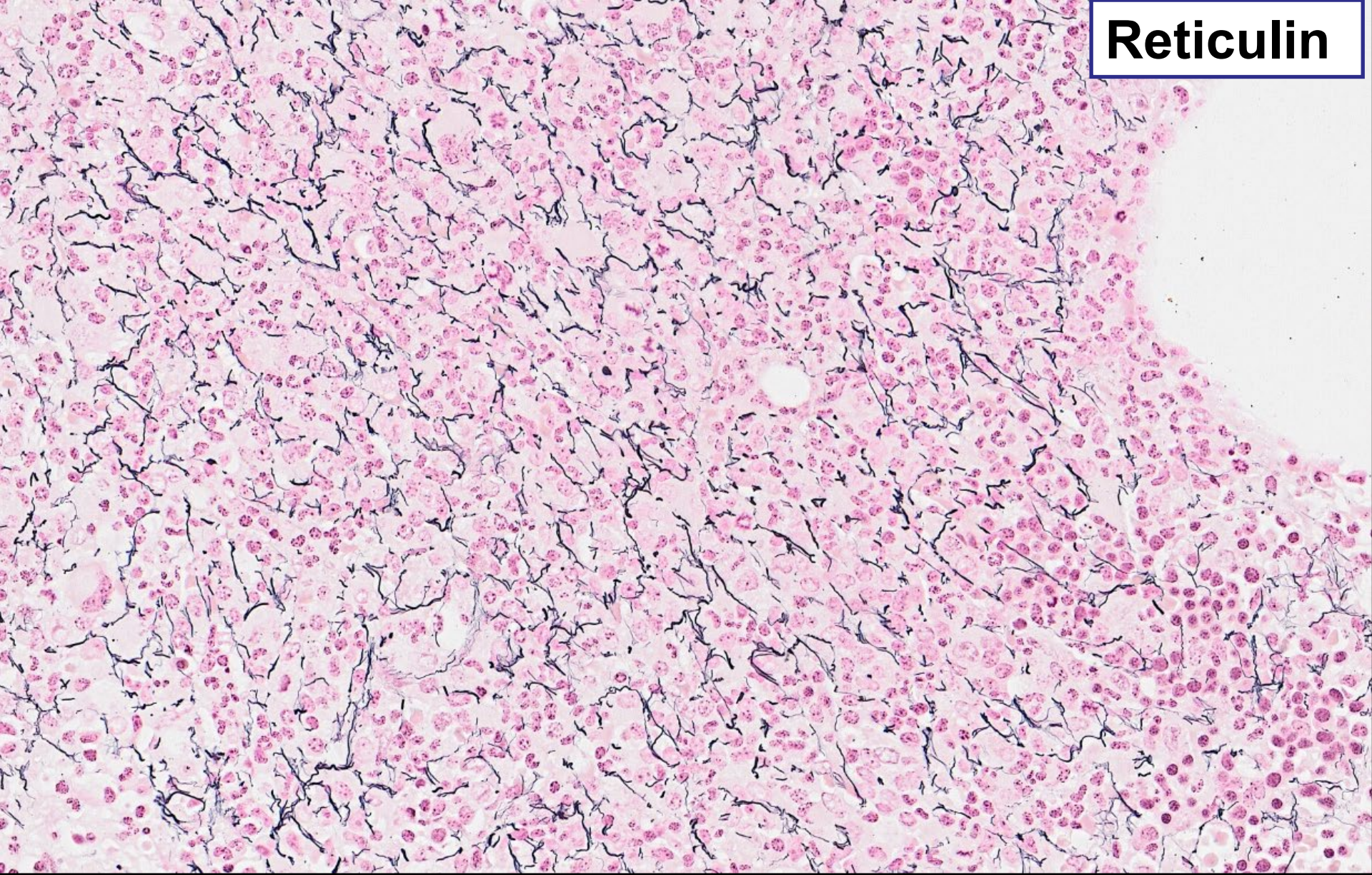
CD138



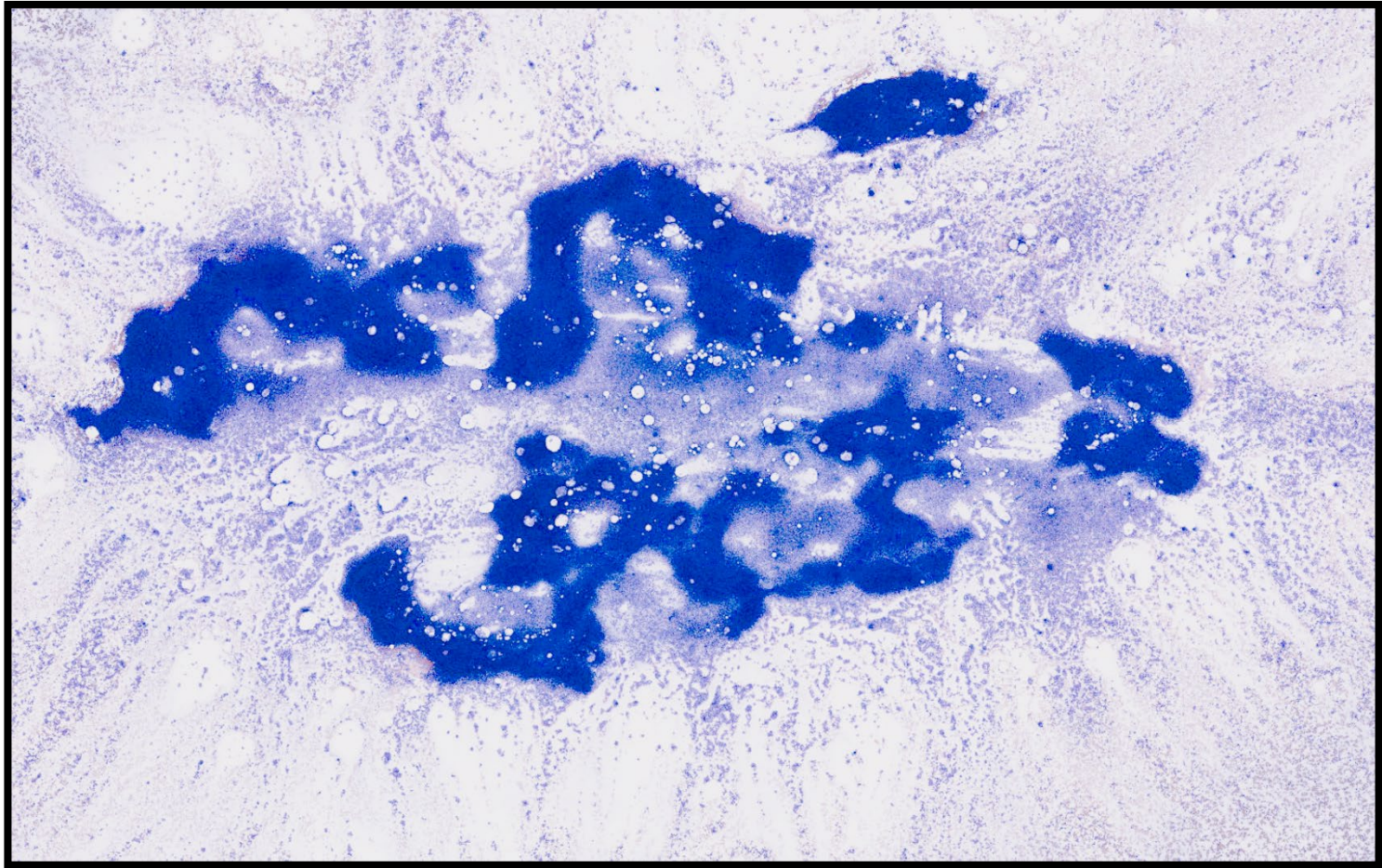
CD56



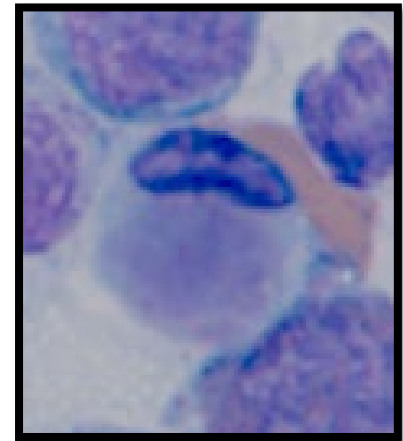
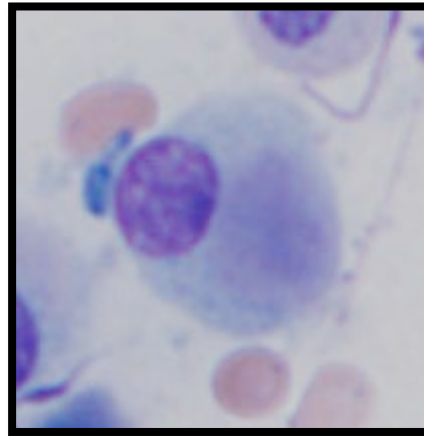
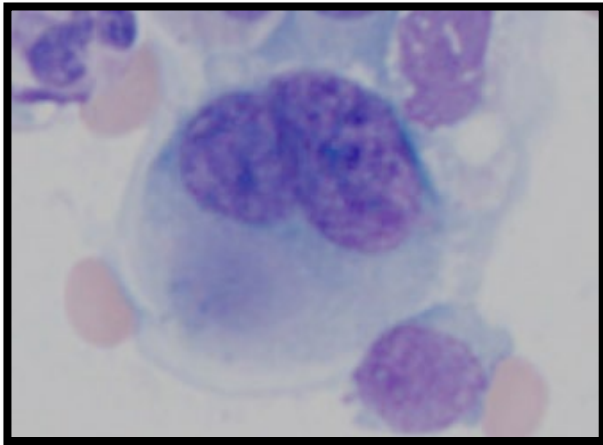
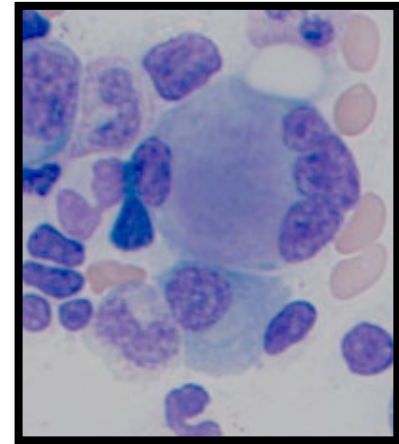
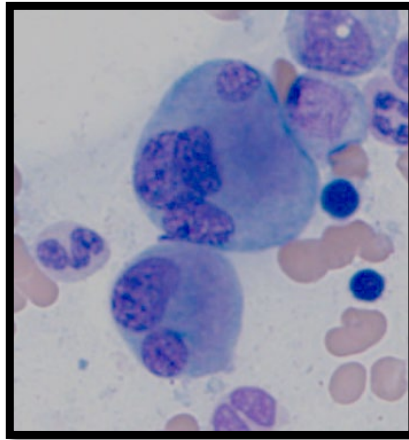
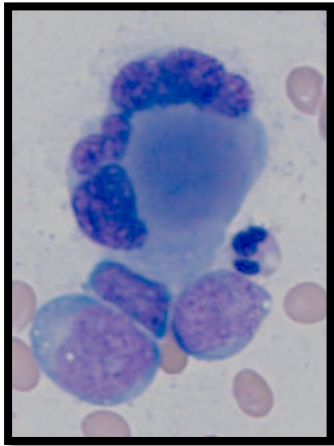
Reticulin



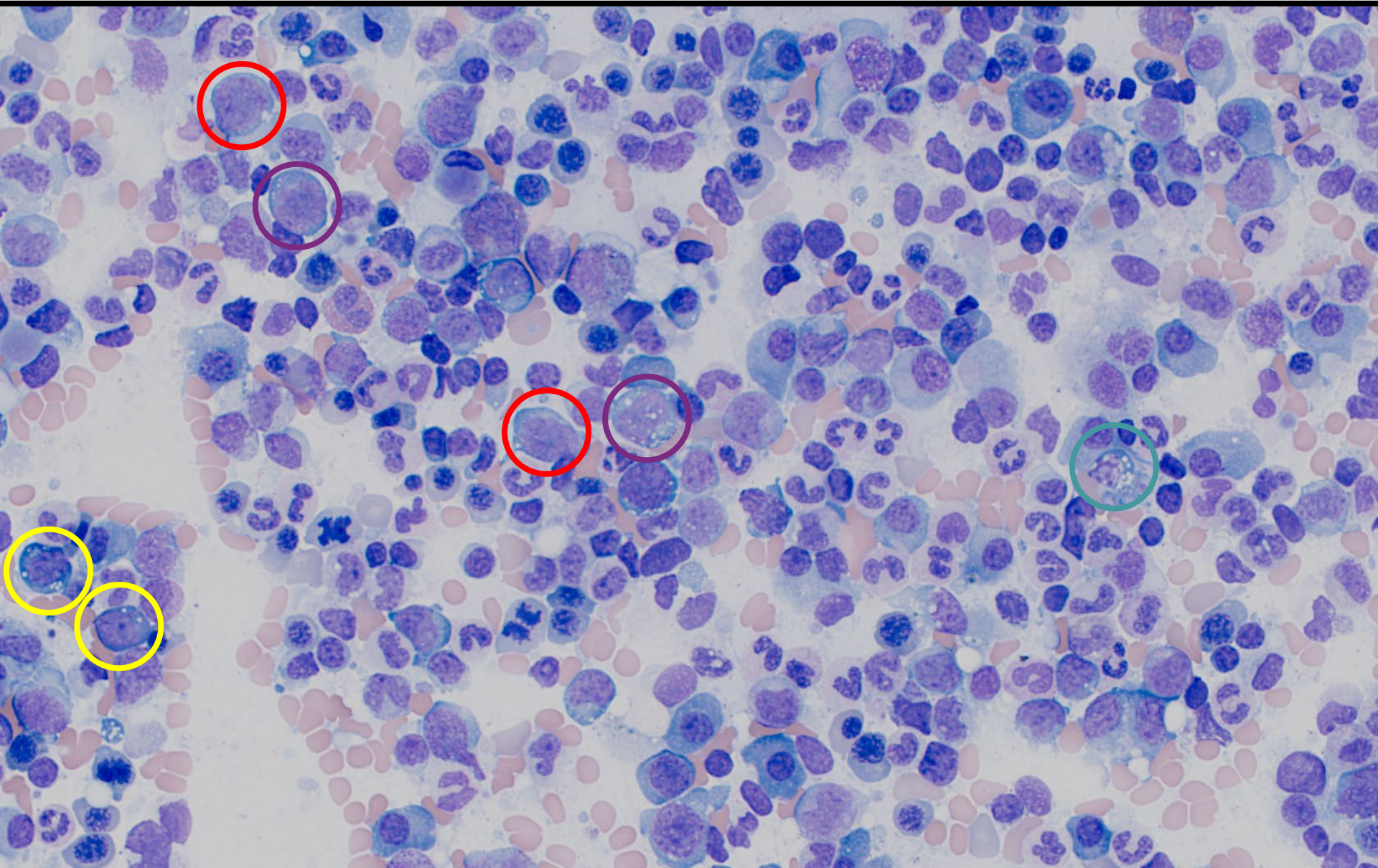
Bone Marrow Aspirate



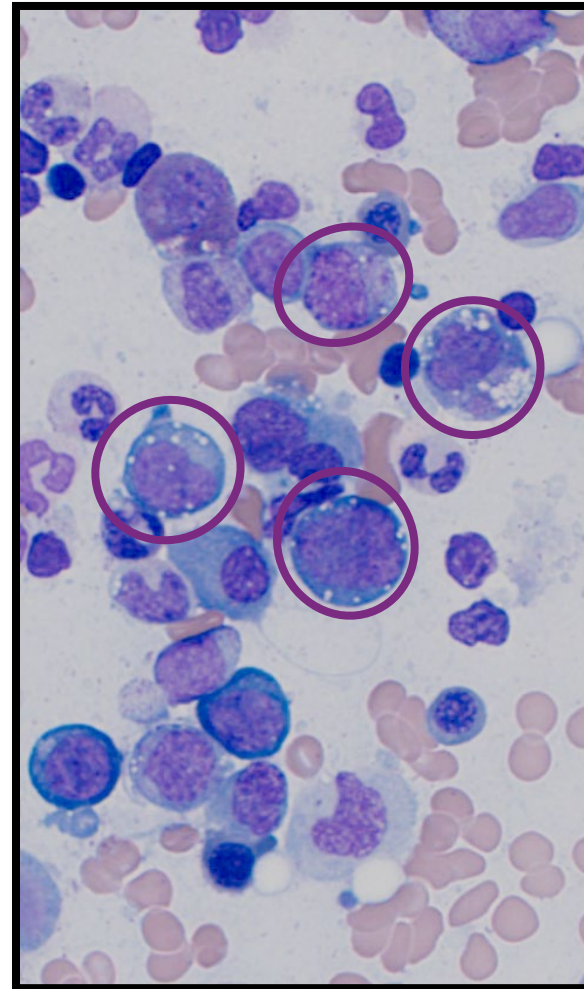
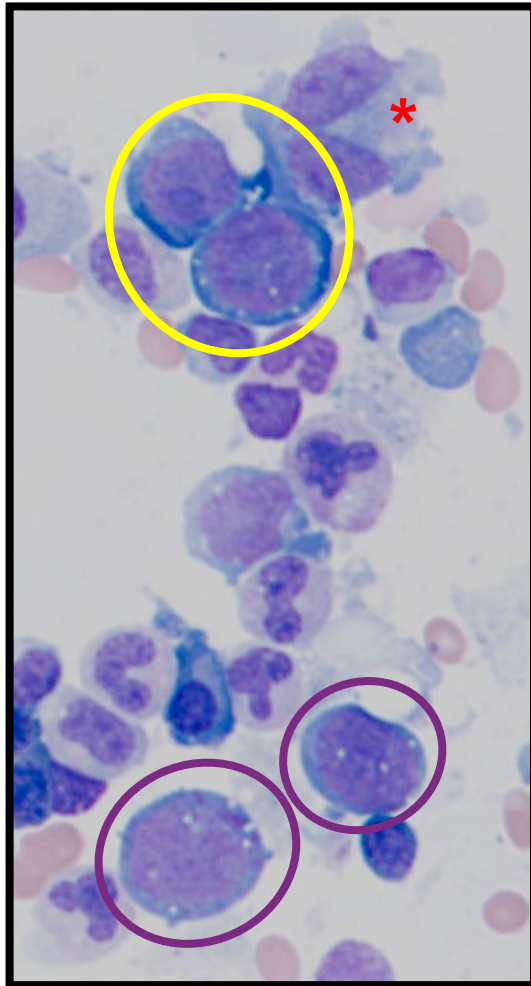
Bone Marrow Aspirate - Dysmegakaryopoiesis



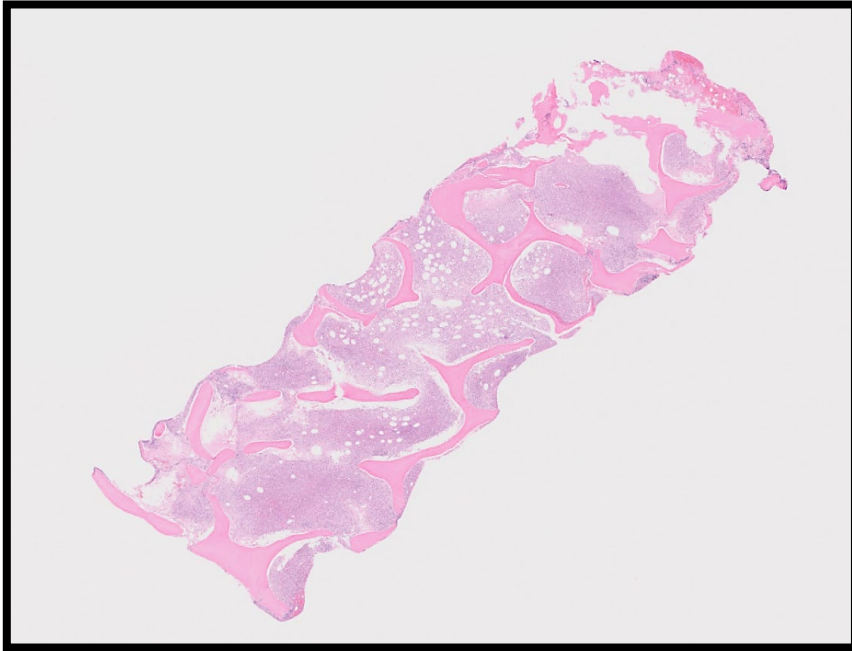
Bone Marrow Aspirate



Bone Marrow Aspirate

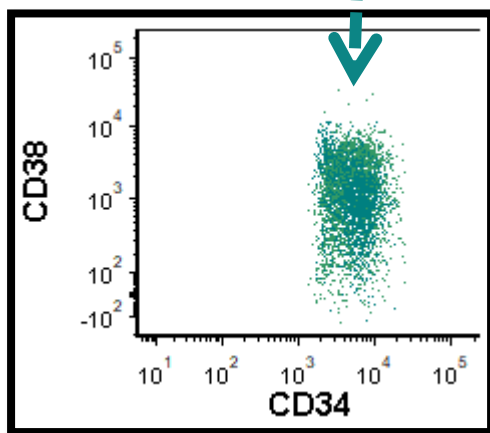
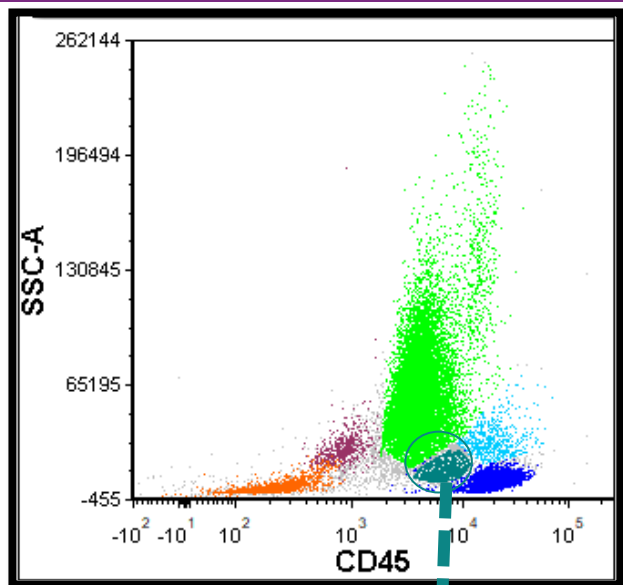


Bone Marrow Biopsy



- Hypercellular marrow (90%)
- Granulocytic hyperplasia
- Megakaryocytic hyperplasia
- Dysmegakaryopoiesis
- Increased number of blasts
- Increased number of plasma cells

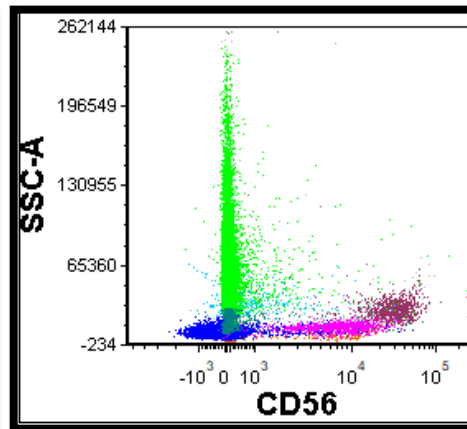
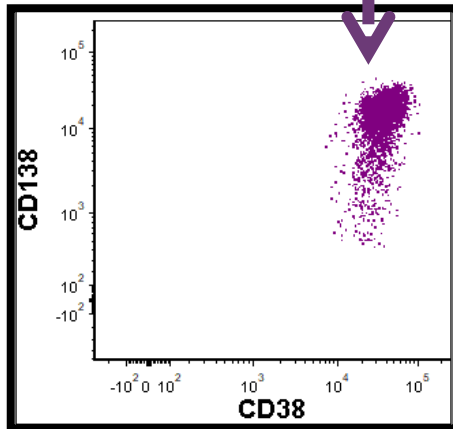
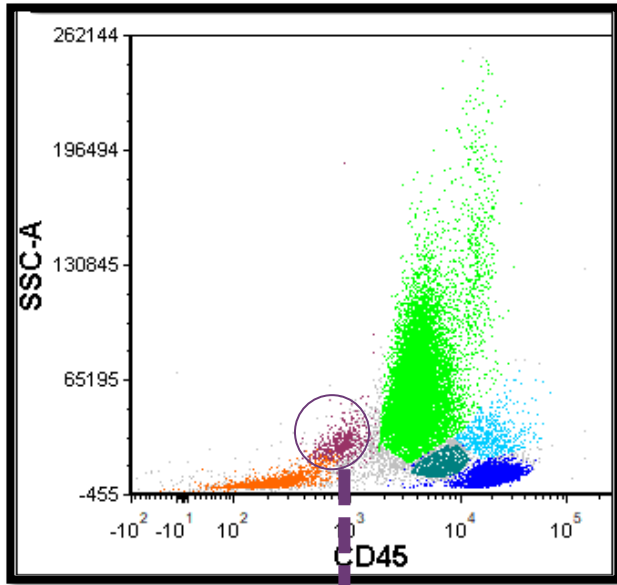
Flow cytometric analysis



Abnormal Blasts

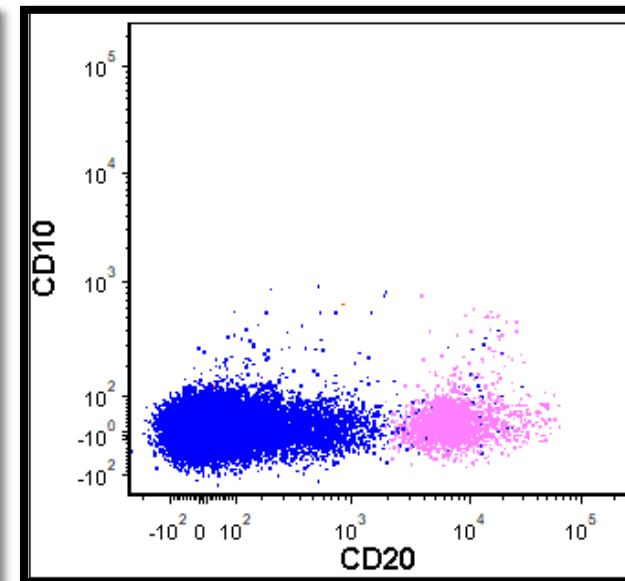
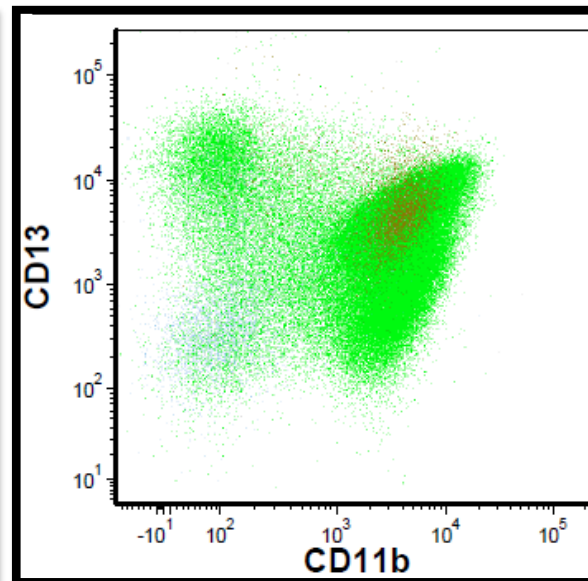
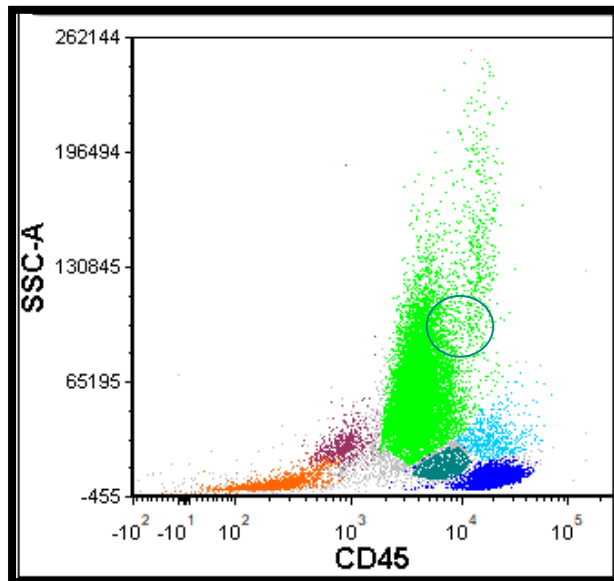
Positive	Negative
CD34	CD38 (downregulated)
CD45	CD56
CD117	Lymphoid markers
CD13 (dim)	
CD33 (bright)	
HLA-DR	

Flow cytometric analysis



Abnormal Plasma cells	
Positive	Negative
CD138	CD19
CD38	CD117
CD56	CD81 (downregulated)
Lambda	CD27 (downregulated)
	CD45

Flow cytometric analysis



Cytogenetic Analysis

- Cytogenetic analysis revealed an abnormal karyotype
 - 46, XY, del (20)(q11.2q13.3)[2] / 46,XY[18]
- Outside FISH results identified
 - ***FGFR3::IGH*** fusion t(4;14)

Molecular (NGS) Analysis

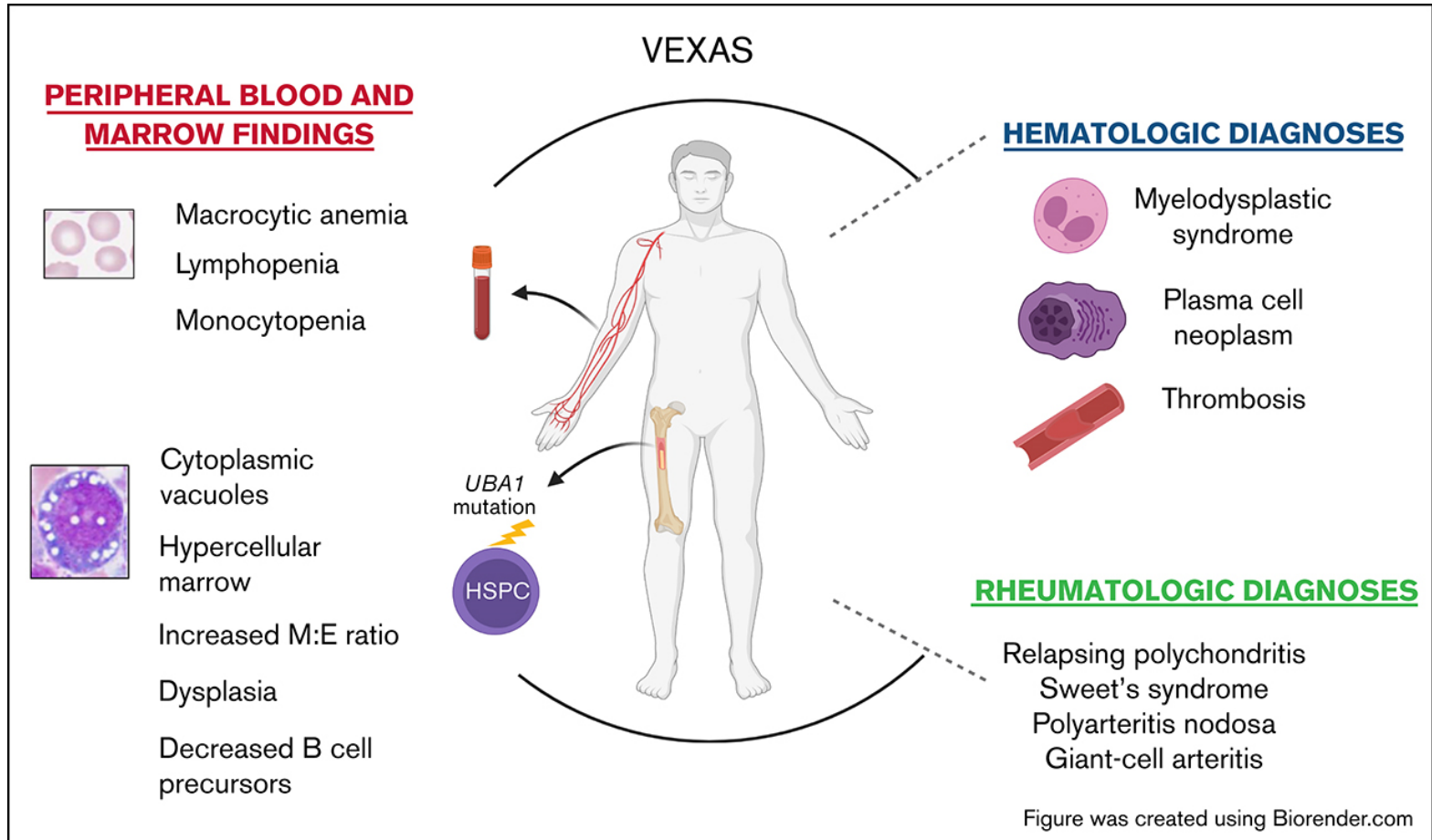
- ***UBA1*** c.118-1 G>C; p.? (VAF 43%)
- ***EZH2*** p.Thr350Aspfs*17 (VAF 4%)
- ***EZH2*** c.247-1 G>A; p.? (VAF 4%)
- ***KDM6A*** p.Asn839Thrfs*28 (VAF 4%)

Integrated Diagnoses

- 1) Hypercellular marrow with multilineage dysplasia and an increased number of blasts (7-9% by CD34), consistent with **Myelodysplastic syndrome with excess blasts (MDS-EB1; ICC) / Myelodysplastic syndrome with increased blasts-1 (MDS-IB1; WHO 5th) associated with VEXAS syndrome.**
- 2) **Plasma cell neoplasm, IgA lambda**

VEXAS Syndrome

(vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic)



Obiorah I. E. et al. *Blood Adv* 2021; 5 (16): 3203–3215

Thank you for your attention.

For additional questions:
Michellykerly.sampaio demelo@nih.gov

