VMX

VETERINARY MEETING & EXPO

The SHOW OF SHOWS

Title Text

WONDERS! WOWS! WISDOM!

JANUARY 13-17 ORLANDO, FL & ONLINE

Presented By:

NAVC

YOUR VETERINARY COMMUNITY

CBC In Cancer Patients: What's Worrying? What's Not? And Why Should I Care?

Guillermo Couto, DVM, DACVIM (SAIM, Oncology)

coutovetconsultants@gmail.com

VMX 2024 VETERINARY MEETING & EXPO

Conflict of Interest Disclosure:

Consultant, IDEXX Laboratories, Inc

Thanks to Dr. Rebekah Mack-Gertig

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The information contained herein is intended to provide general guidance only. As with any diagnosis or treatment, you should use clinical discretion with each patient based on a complete evaluation of the patient, including history, physical presentation, and complete laboratory data. With respect to any drug therapy or monitoring program, you should refer to product inserts for a complete description of dosages, indications, interactions, and cautions. Diagnosis and treatment decisions are the ultimate responsibility of the primary care veterinarian.

CBC In Oncology

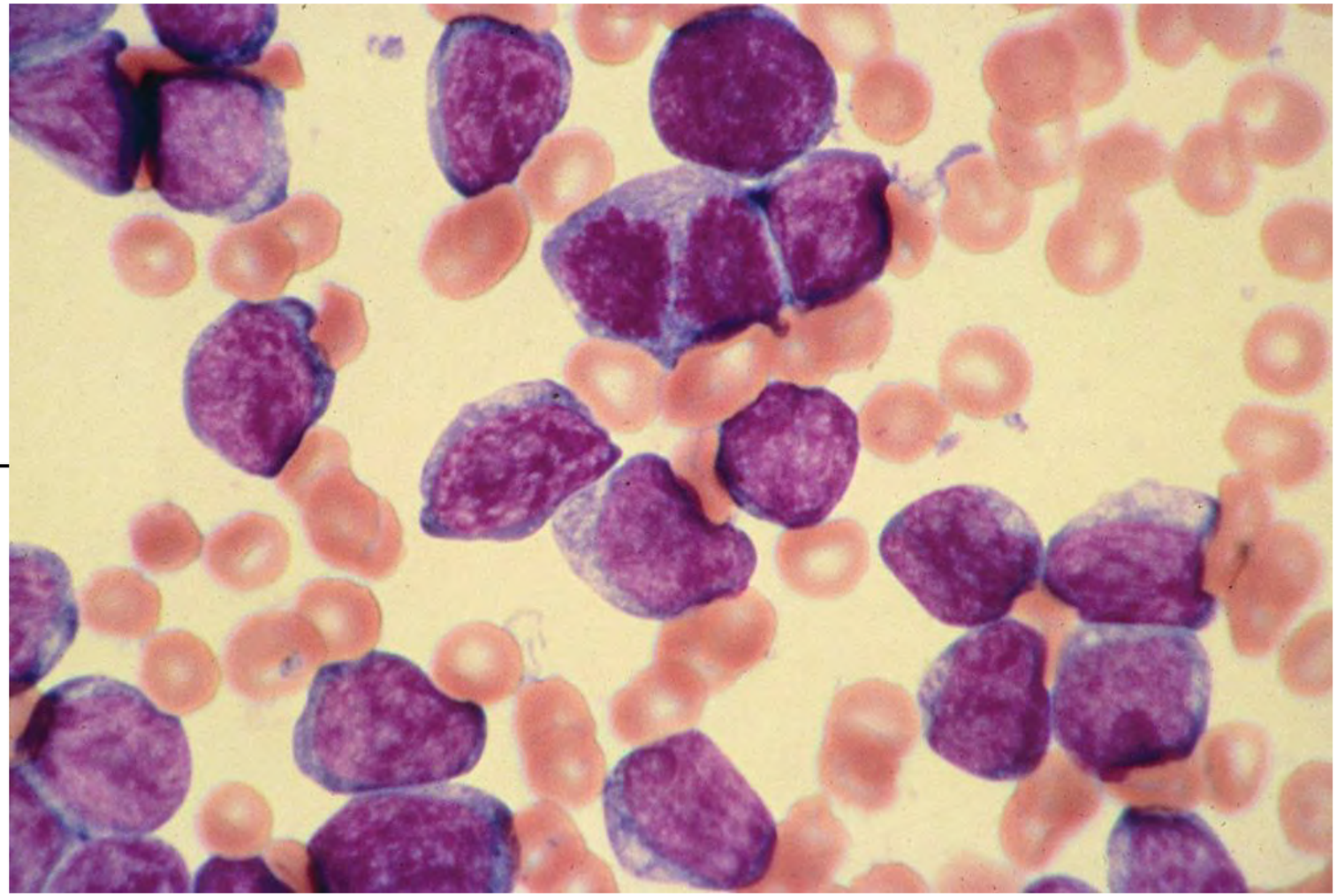
- Provides a diagnosis
- Suggests subclinical neoplasia
- Staging?
- Monitoring response to treatment
- Monitoring chemotherapy
- Common hematologic abnormalities

CBC In Oncology

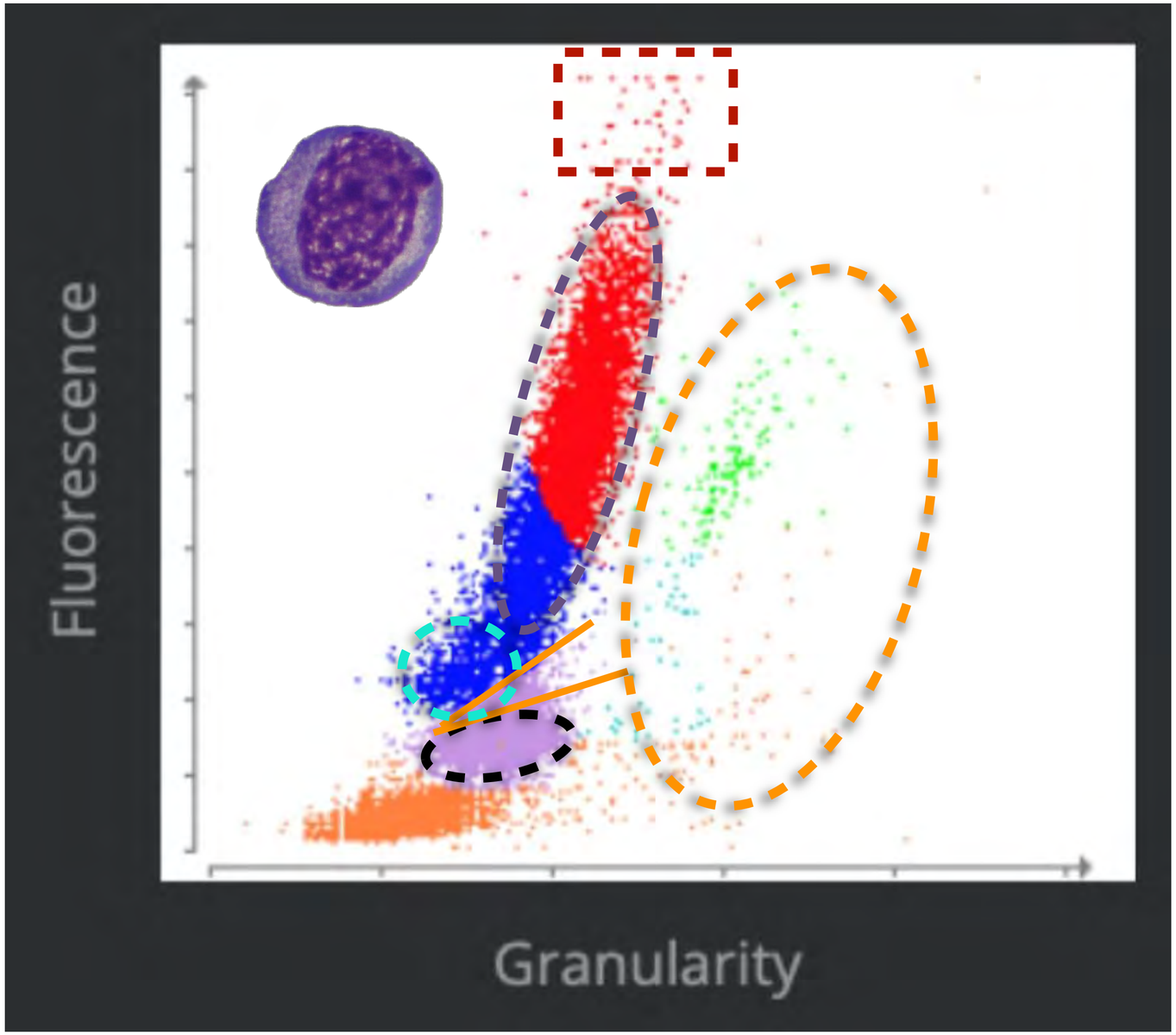
- Provides a diagnosis
- Suggests subclinical neoplasia
- Staging?Monitoring response to Rx
- Monitoring chemotherapy

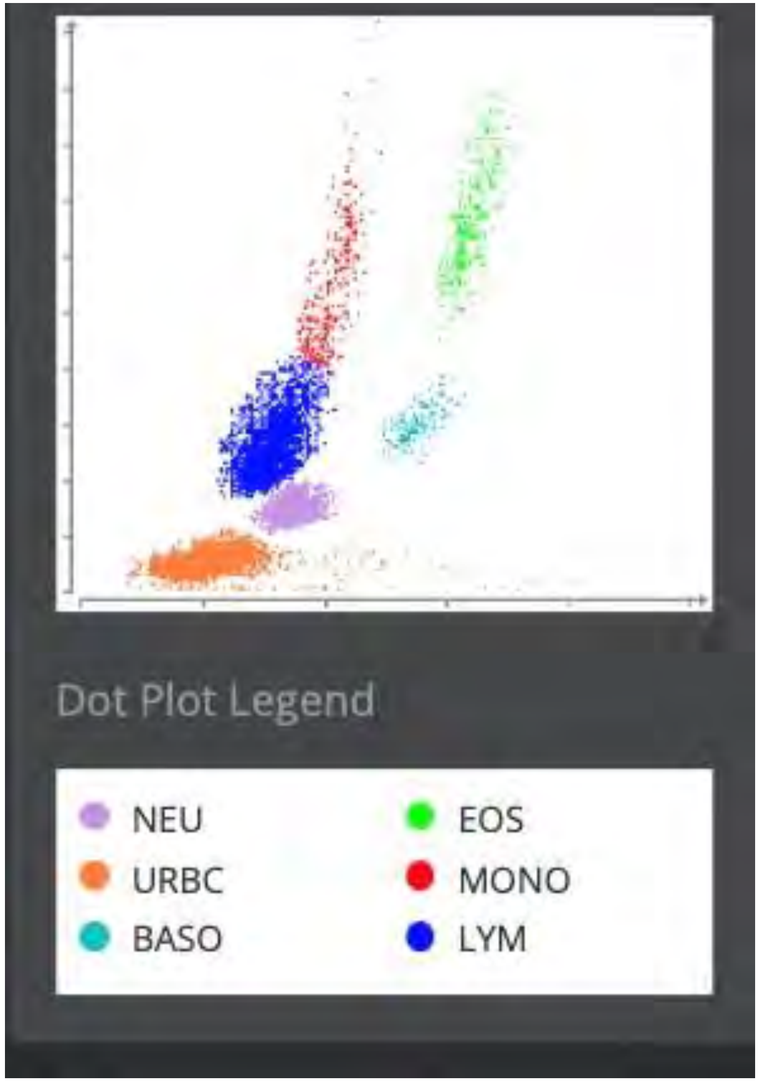
CBC In Oncology

- Provides a diagno



Simon-WBC Dot Plots





Drs. Kate Sycamore and Jason Couto

CBC In Oncology

- Provides a diagnosis
- Suggests subclinical neoplasia
- Staging?Monitoring response to Rx
- Monitoring chemotherapy
- Common hematologic abnormalities

CBC In Oncology

- Suggests subclinical neoplasia
  - Anemia/erythrocytosis
  - Leukopenia
    - Neutropenia
  - Leukocytosis
    - Neutrophilia, lymphocytosis, eosinophilia, monocytosis
  - Thrombocytopenia/thrombocytosis
  - Bi- or pancytopenia

CBC In Oncology

- Provides a diagnosis
- Suggests subclinical neoplasia
- Staging?
- Monitoring response to Rx
- Monitoring chemotherapy
- Common hematologic abnormalities

CBC In Oncology

- Staging
  - Pancytopenia lymphoma patient

CBC In Oncology

- Provides a diagnosis
- Suggests subclinical neoplasia
- Staging?
- Monitoring response to Rx
- Monitoring chemotherapy
- Common hematologic abnormalities

CBC In Oncology

- Monitoring response to Rx
  - resolution of cytopenia/-cytosis

CBC In Oncology

- Provides a diagnosis
- Suggests subclinical neoplasia
- Staging?
- Monitoring response to Rx
- Monitoring chemotherapy
- Common hematologic abnormalities

CBC In Oncology

- Monitoring chemotherapy
  - Neutropenia
  - Thrombocytopenia
  - Iron-deficiency anemia

CBC In Oncology

- Monitoring chemotherapy
  - Neutrophil "cut-off" for chemotherapy
    - 2.5 X 10^9/L???
    - 1.0 X 10^9/L???
    - Let common sense prevail…

CBC In Oncology

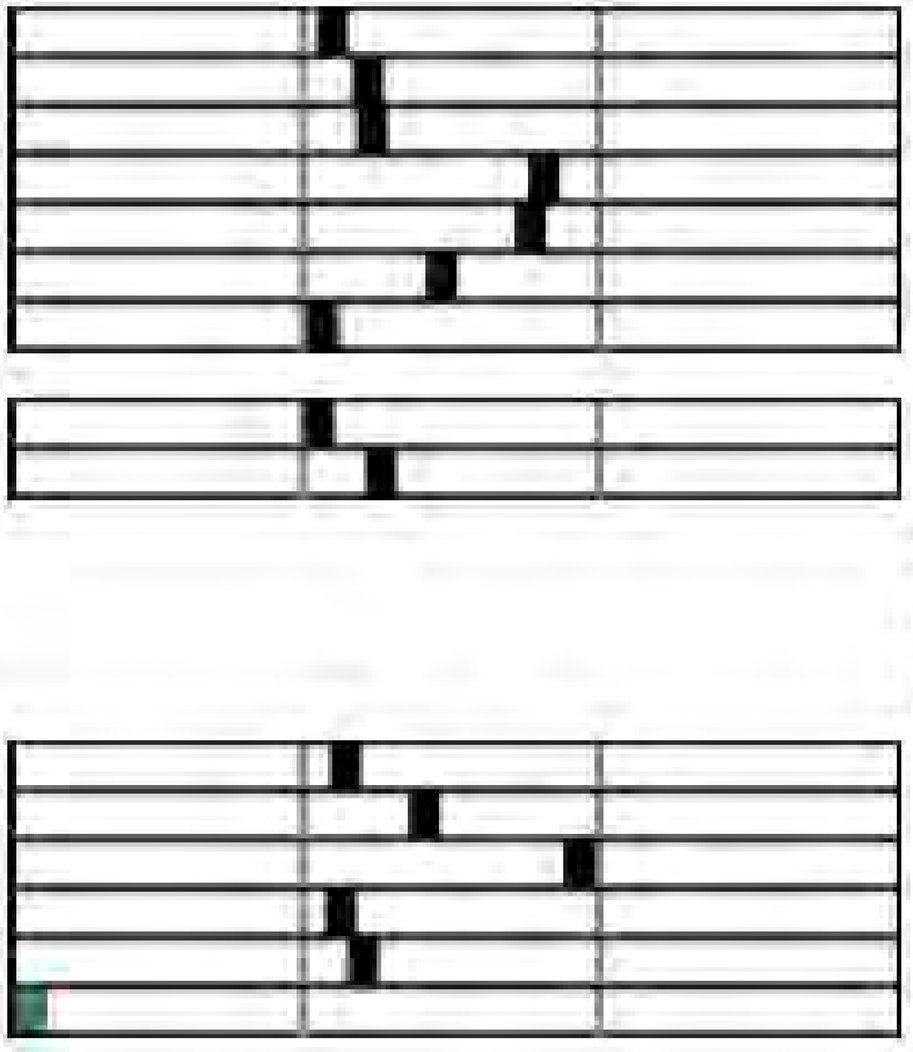
- Monitoring chemotherapy
  - Thrombocytopenia
    - 50 X 10^9/L???
    - Is it real???

CBC In Oncology

- "Chewy", 4, MC, Mixed breed dog
  - On CHOP for multicentric lymphoma
  - Here for VINCRISTINE today

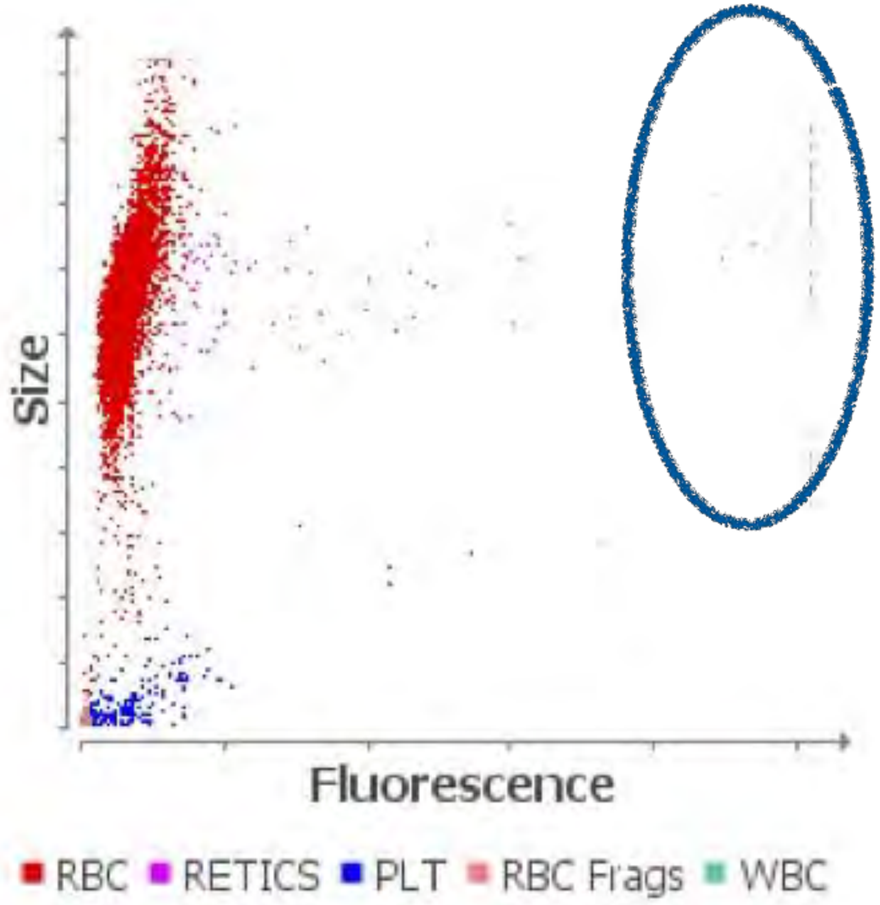
Test	Results	Reference Interval	LOW	NORMAL	HIGH	6/26/12 10:35 AM
ProCyte Dx (July 13, 2012 1:06 PM)						
RBC	5.97 M/µL	5.65 - 8.87				6.47 M/µL
HCT	42.5 %	37.3 - 61.7				46.0 %
HGB	14.8 g/dL	13.1 - 20.5				16.1 g/dL
MCV	71.2 fL	61.6 - 73.5				71.1 fL
MCH	24.8 pg	21.2 - 25.9				24.9 pg
MCHC	34.8 g/dL	32.0 - 37.9				35.0 g/dL
RDW	14.2 %	13.6 - 21.7				15.3 %
%RETIC	0.2 %					0.3 %
RETIC	13.7 K/µL	10.0 - 110.0				19.4 K/µL
WBC	* 8.15 K/µL	5.05 - 16.76				9.17 K/µL
%NEU	* 50.8 %					75.4 %
%LYM	* 33.6 %					15.2 %
%MONO	* 12.9 %					6.5 %
%EOS	* 2.5 %					2.4 %
%BASO	* 0.2 %					0.5 %
NEU	* 4.14 K/µL	2.95 - 11.64				6.91 K/µL
LYM	* 2.74 K/µL	1.05 - 5.10				1.39 K/µL
MONO	* 1.05 K/µL	0.18 - 1.12				0.60 K/µL
EOS	* 0.20 K/µL	0.06 - 1.23				0.22 K/µL
BASO	* 0.02 K/µL	0.00 - 0.10				0.05 K/µL
PLT	* 24 K/µL	145 - 456	LOW			176 K/µL
MPV	--.- fL	8.7 - 13.2				10.9 fL
PDW	--.- fL	9.1 - 19.4				12.7 fL
PCT	--.- %	0.14 - 0.46				0.19 %

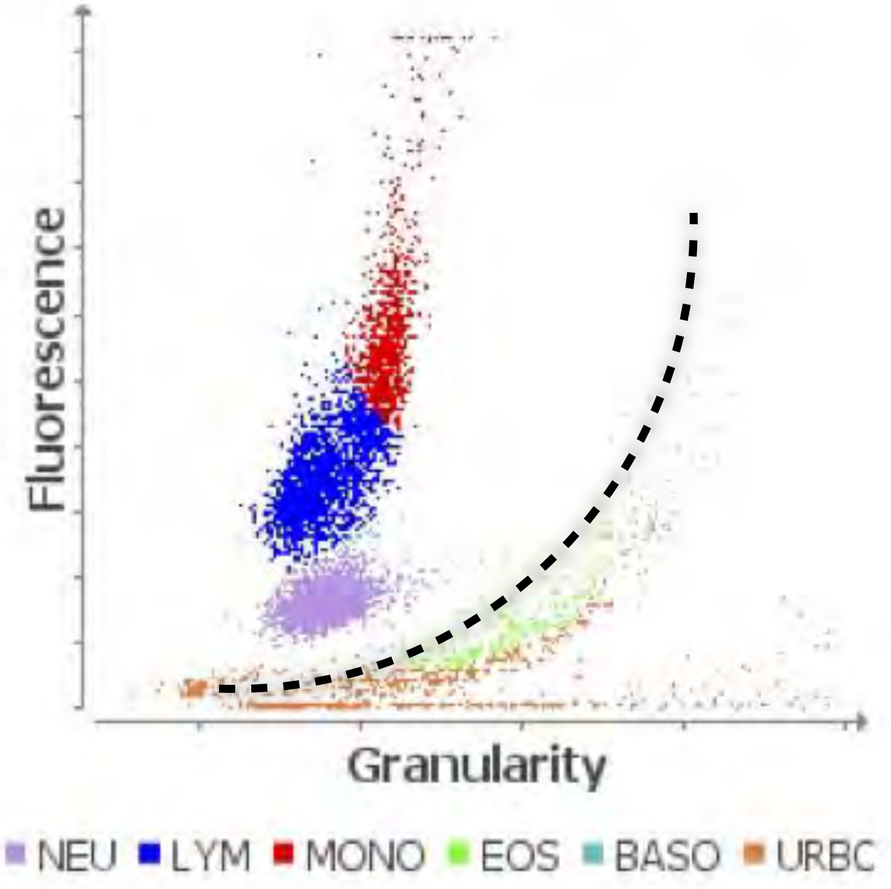
PLT Aggregates Detected



PLT	24 K/uL	148 - 484	LOW
MPV	--- fL	8.7 - 13.2	
PDW	--- fL	9.1 - 19.4	
PCT	--- %	0.14 - 0.46	

PLT Aggregates Detected





CBC In Oncology

- "Chewy", 4, MC, Mixed breed dog
  - On CHOP for multicentric lymphoma
  - Here for VINCRISTINE today
  - And he got it!

The moral of the story: All "thrombocytopenias" should have a blood smear or cytogram review

CBC In Oncology

- Provides a diagnosis
- Suggests subclinical neoplasia
- Staging?
- Monitoring response to Rx
- Monitoring chemotherapy
- Common hematologic abnormalities

CBC In Oncology

- Red blood cells
- White blood cells
- Platelets

CBC In Oncology

- Red blood cells
  - Anemia
  - Erythrocytosis

Anemia

Regenerative

"Macrocytic
Hypochromic"

Blood loss
Hemolysis

Semi-regenerative

Microcytic
Hypochromic
Retics
Lots of platelets

Iron deficiency

Non regenerative

Normocytic
Normochromic

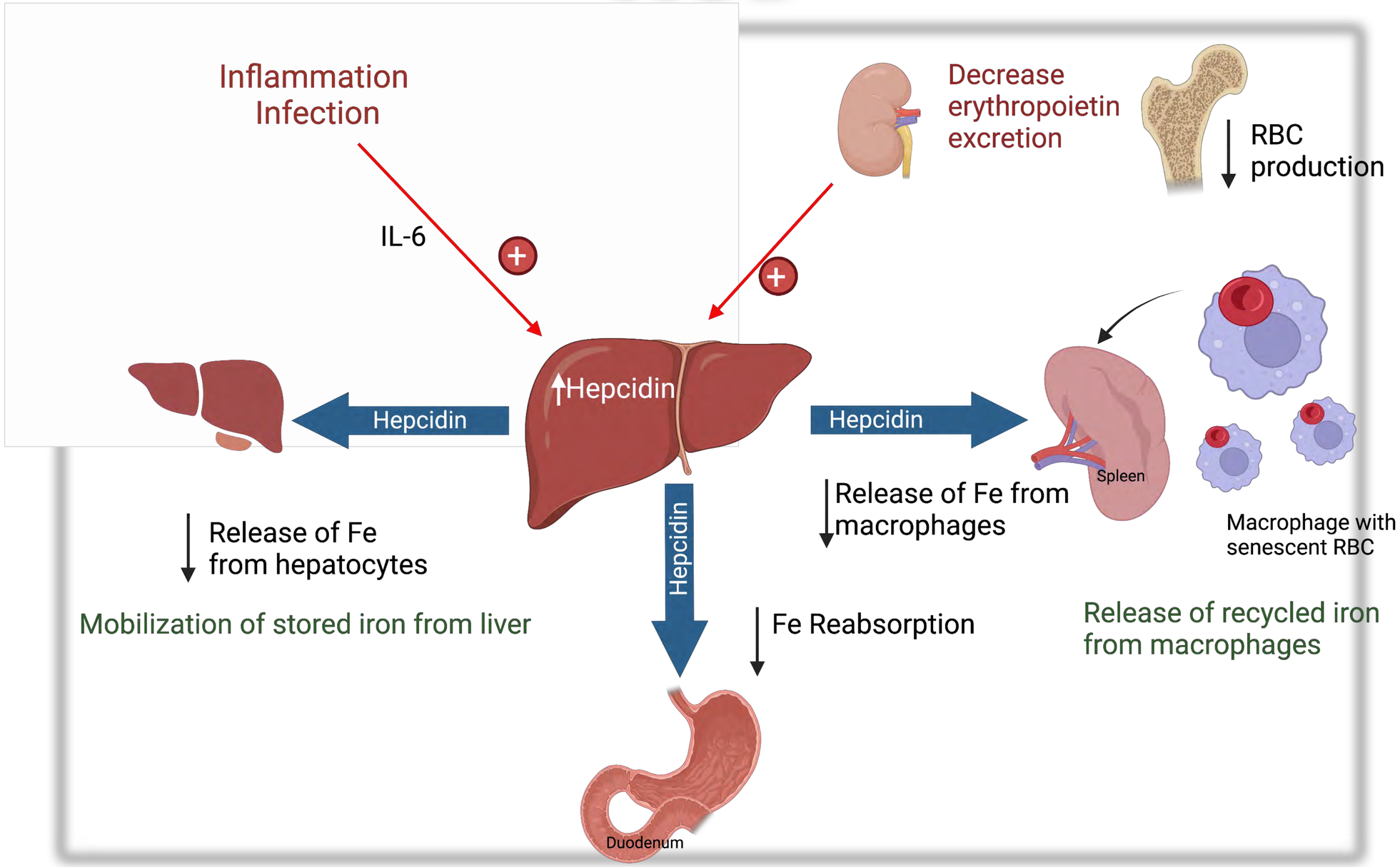
ACD
CKD
BM
(Endocrine)

With impedance analyzers,
90% of regenerative anemias
are NOT macrocytic, hypochromic

Anemia Of Chronic Disease (ACD)

- Most common anemia in cancer patients
- Mild, normocytic, normochromic
- Chronic cytokine->hepcidin release
- Fe “hoarding” by macrophages in BM/decreased Fe absorption
- Clinically relevant?

ACD


Inflammation
Infection
IL-6
Decrease
erythropoietin
excretion
RBC
production
Hepcidin
Hepcidin
Hepcidin
Hepcidin
Release of Fe
from hepatocytes
Mobilization of stored iron from liver
Release of Fe from
macrophages
Spleen
Macrophage with
senescent RBC
Release of recycled iron
from macrophages
Fe Reabsorption
Duodenum

Anemia

Regenerative

"Macrocytic
Hypochromic"

Blood loss
Hemolysis

Semi-regenerative

Microcytic
Hypochromic
Retics
Lots of platelets

Iron deficiency

Non regenerative

Normocytic
Normochromic

ACD
CKD
BM
(Endocrine)

Which ones are common in cancer patients?

Anemia

Regenerative

"Macrocytic Hypochromic"

Blood loss
Hemolysis

Semi-regenerative

Microcytic
Hypochromic
Retics
Lots of platelets

Iron deficiency

Non regenerative

Normocytic
Normochromic

ACD
CKD
BM
(Endocrine)

A dog with HSA has…

Anemia

Regenerative

"Macrocytic Hypochromic"

Blood loss
Hemolysis

Semi-regenerative

Microcytic
Hypochromic
Retics
Lots of platelets

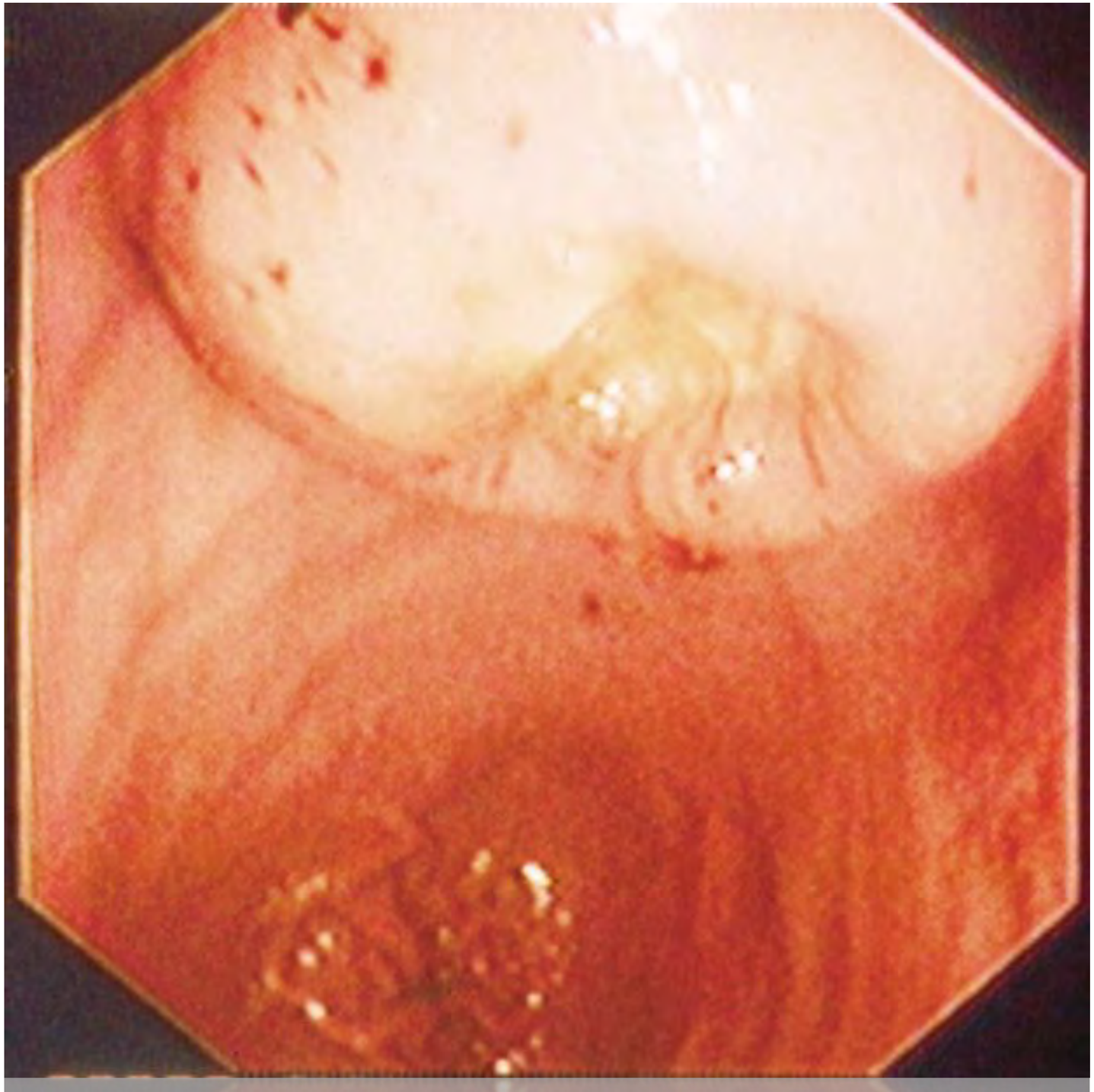
Iron deficiency

Non regenerative

Normocytic
Normochromic

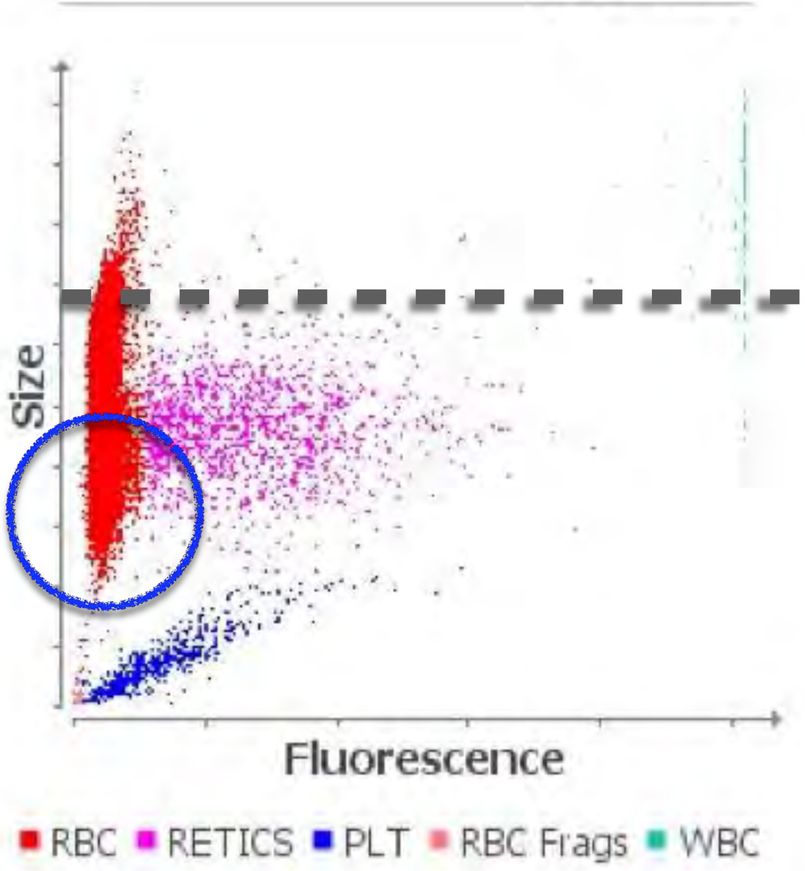
ACD
CKD
BM
(Endocrine)

A dog with an intestinal tumor has…

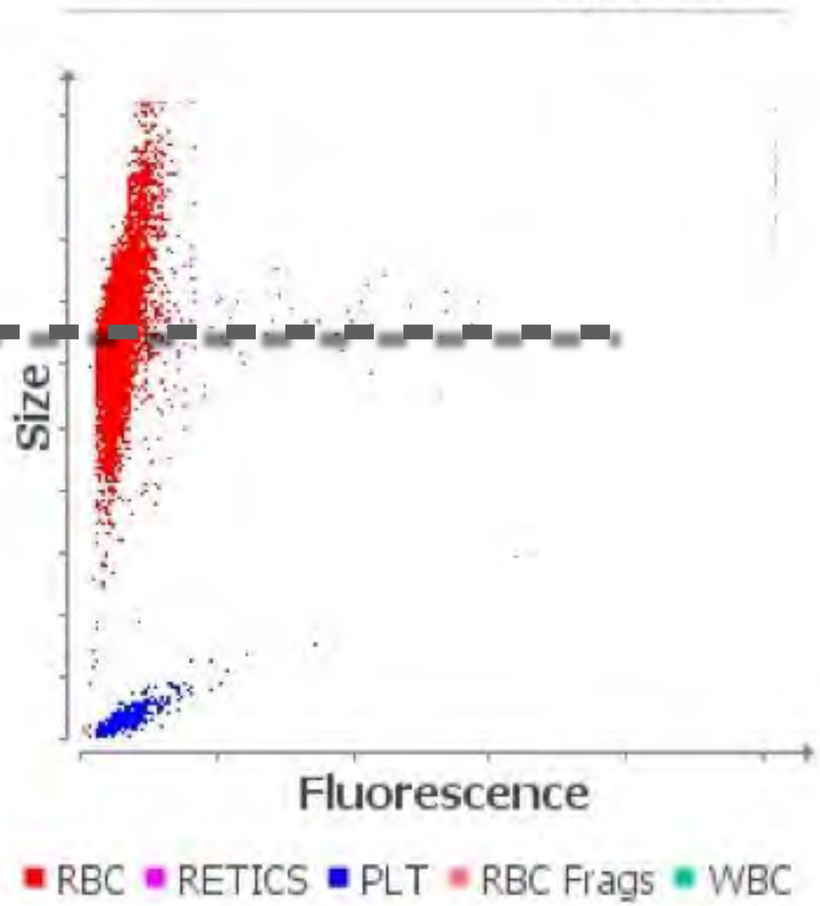


Jejunal GIST

Patient



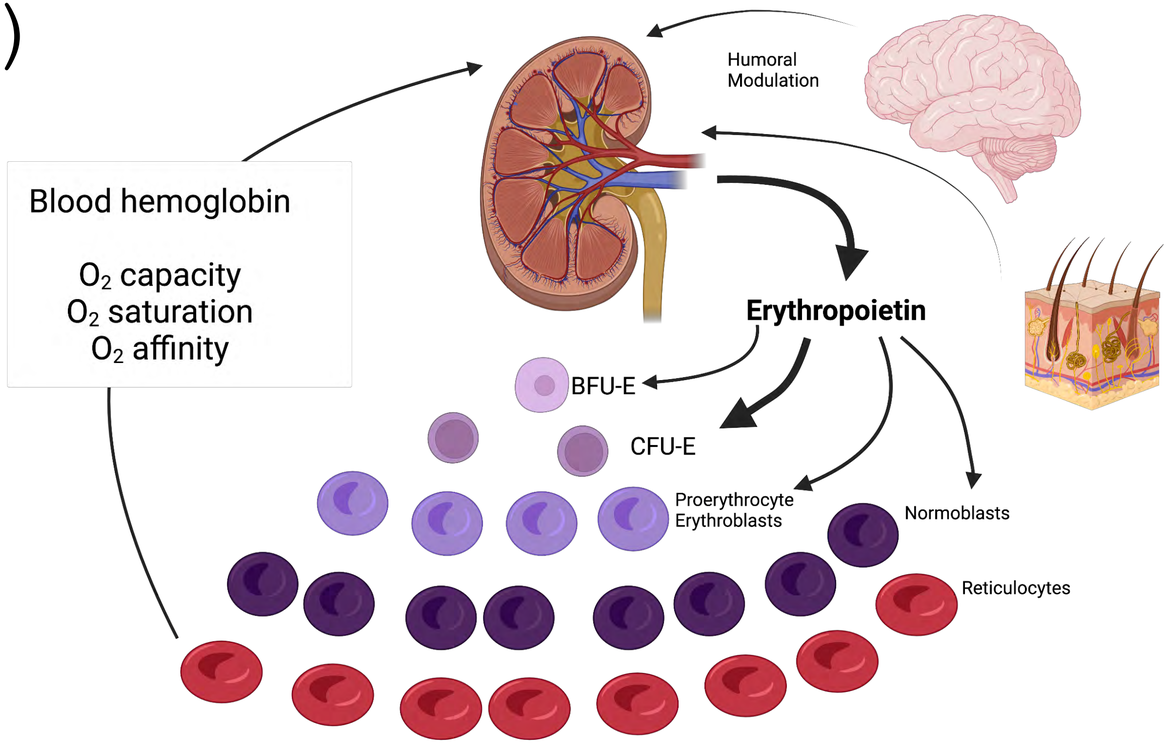
Normal



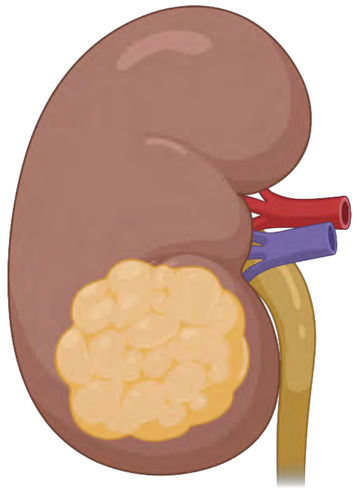
Erythrocytosis

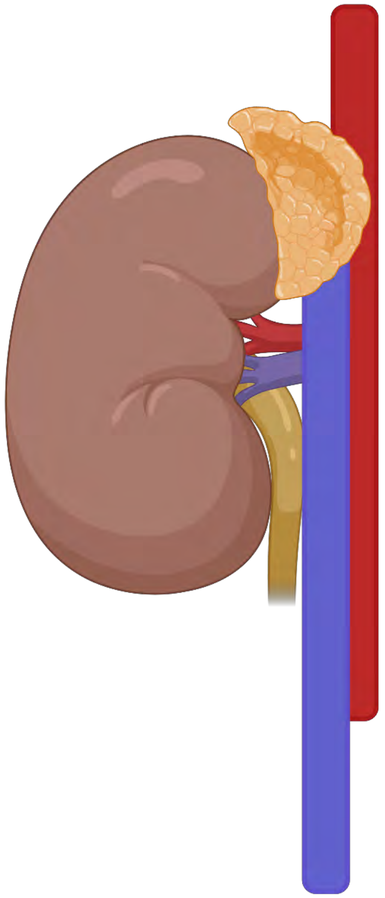
- Appropriate or inappropriate release of EPO

- Autonomous RBC proliferation (Polycythemia vera)



Erythrocytosis

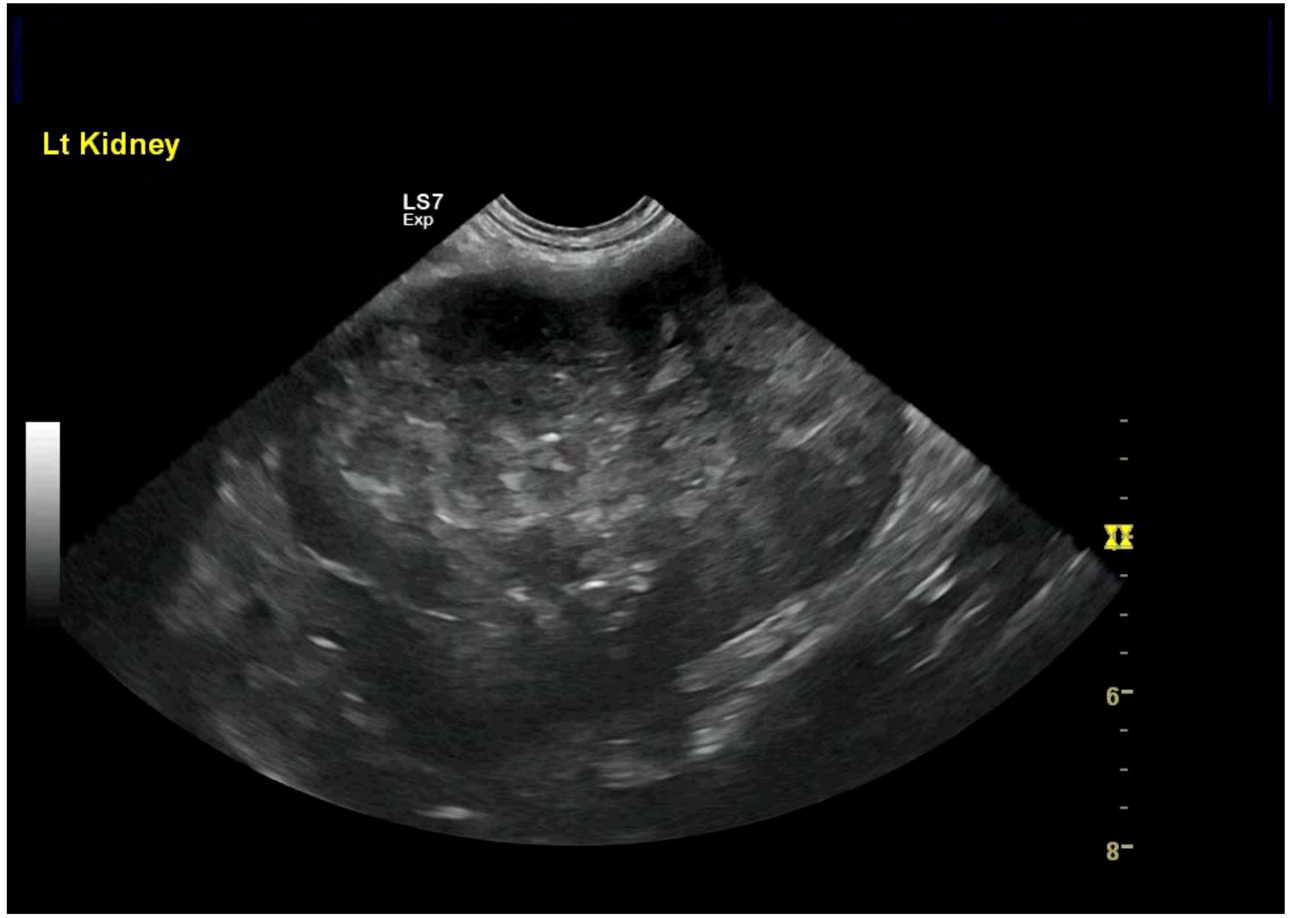




- Renal masses
- Extrarenal compression (pheo)

Erythrocytosis

- Tumor EPO production:
  - Renal carcinomas
  - Nasal fibrosarcoma
  - Any other tumor



CBC in oncology

White blood cells

01 **Neutrophils**
Neutrophilia/neutropenia

02 **Lymphocytes**
Lymphocytosis

03 **Eosinophils**
Eosinophilia

04 **Monocytes**
Monocytosis

Neutrophils

Neutrophilia

+ Necrosis
+ Systemic inflammation
+ Tumor G-CSF/ GM-CSF production

Neutropenia

+ BM involvement
+ Immune-mediated
+ Chemotherapy

White blood cells

Lymphocytosis

+ Leukemia
+ (CLL vs ALL)
+ Lymphoma
+ Thymoma

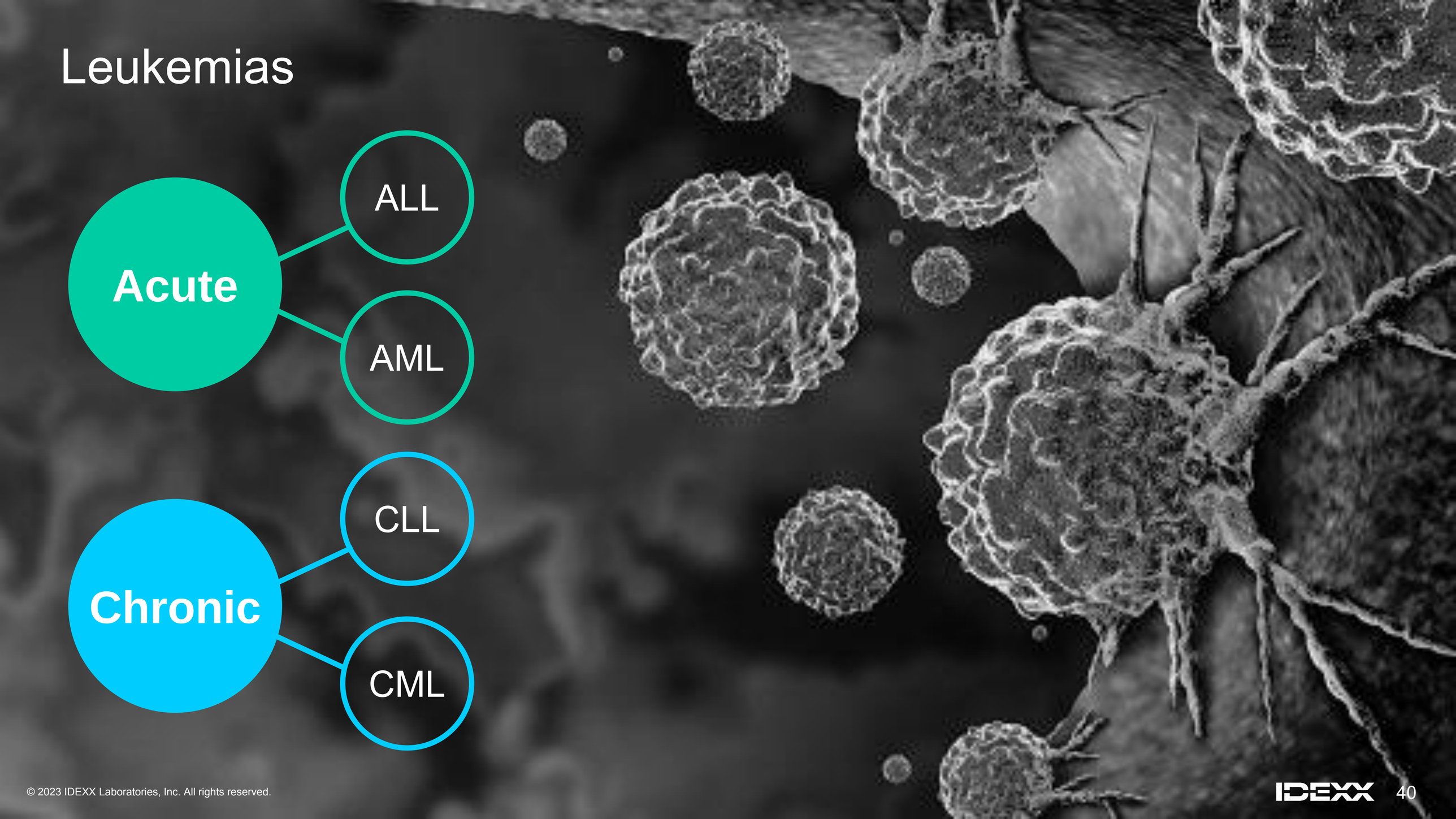
Eosinophilia

+ Lymphoma
+ SCCs
+ Other CAs

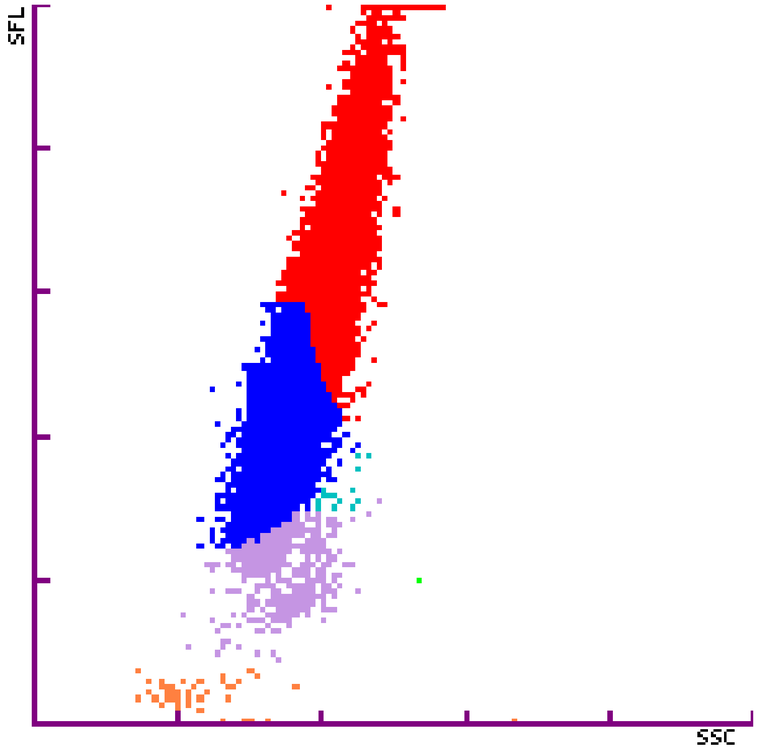
Monocytosis

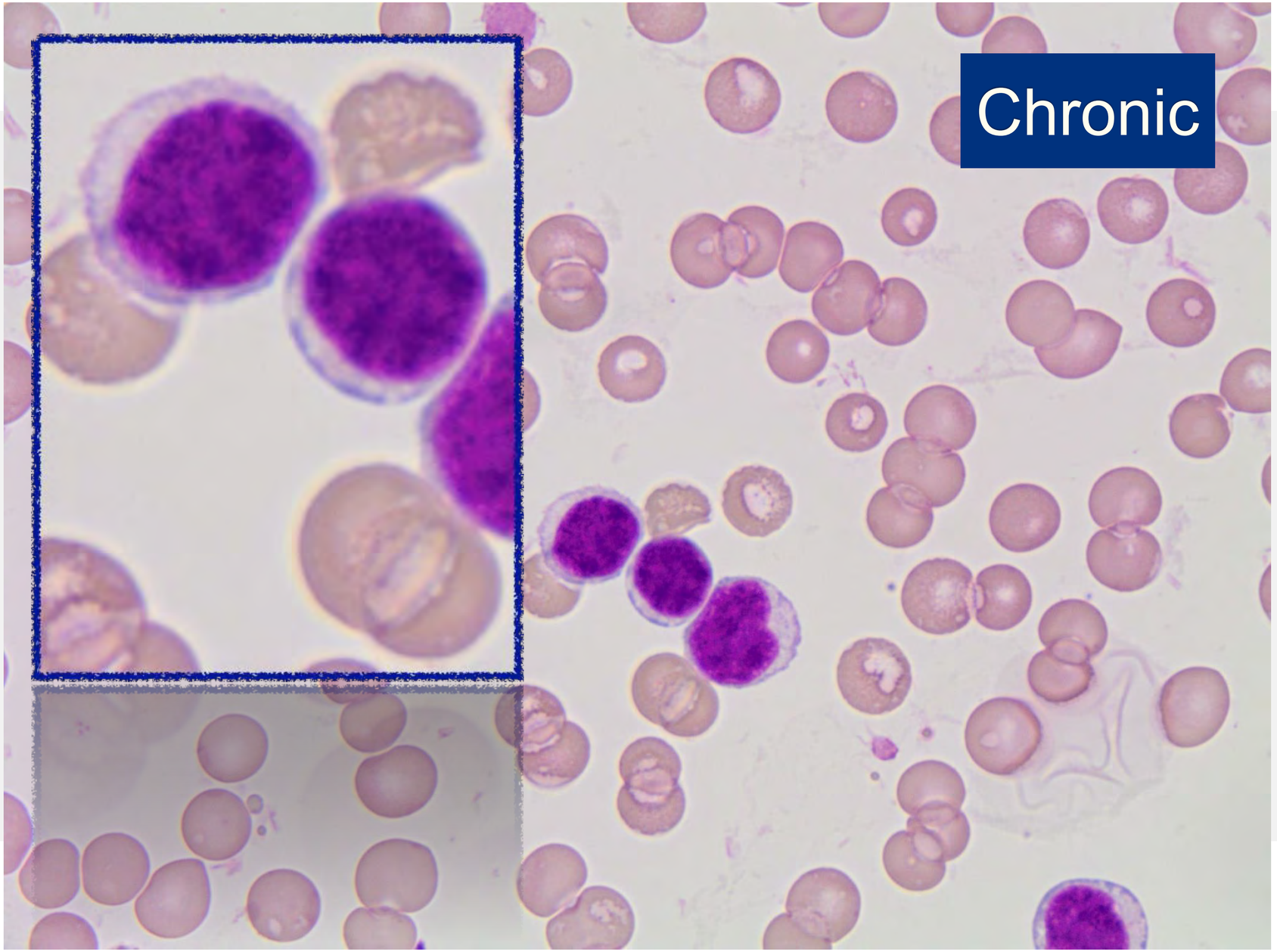
+ Lymphoma
+ Necrotic tumors
+ “Not monocytes”

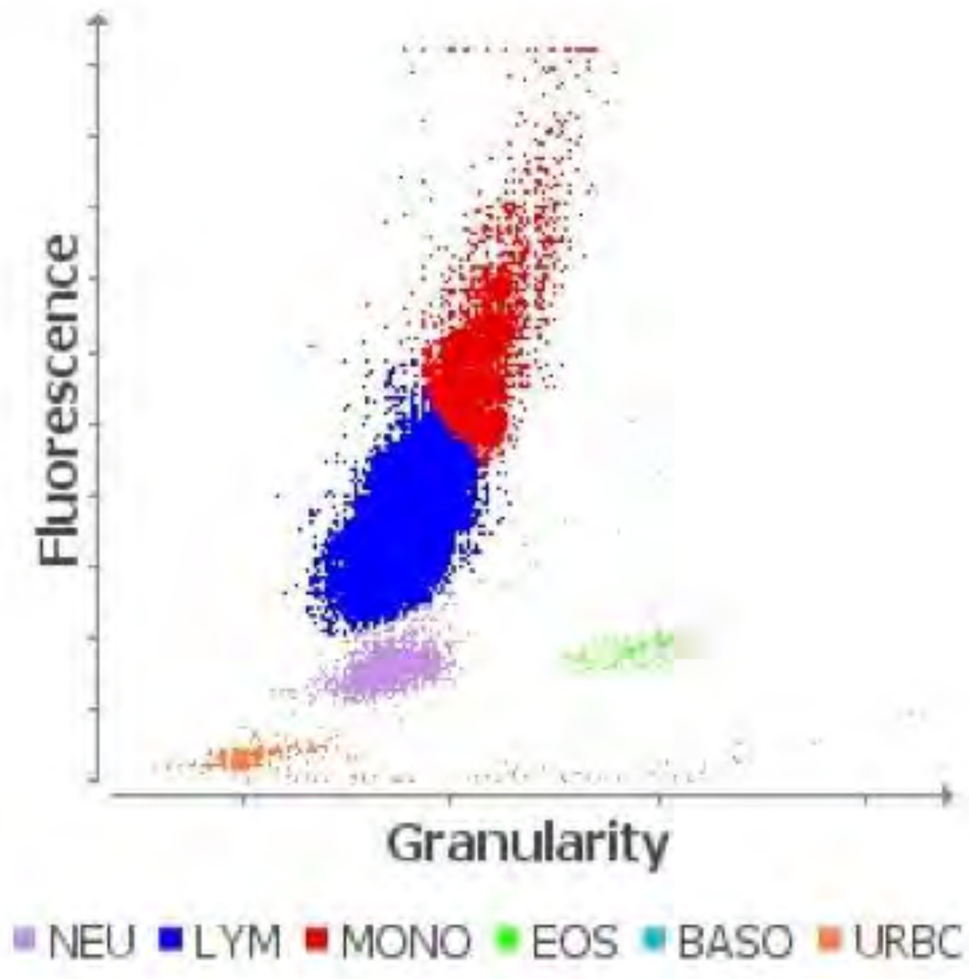
Leukemias

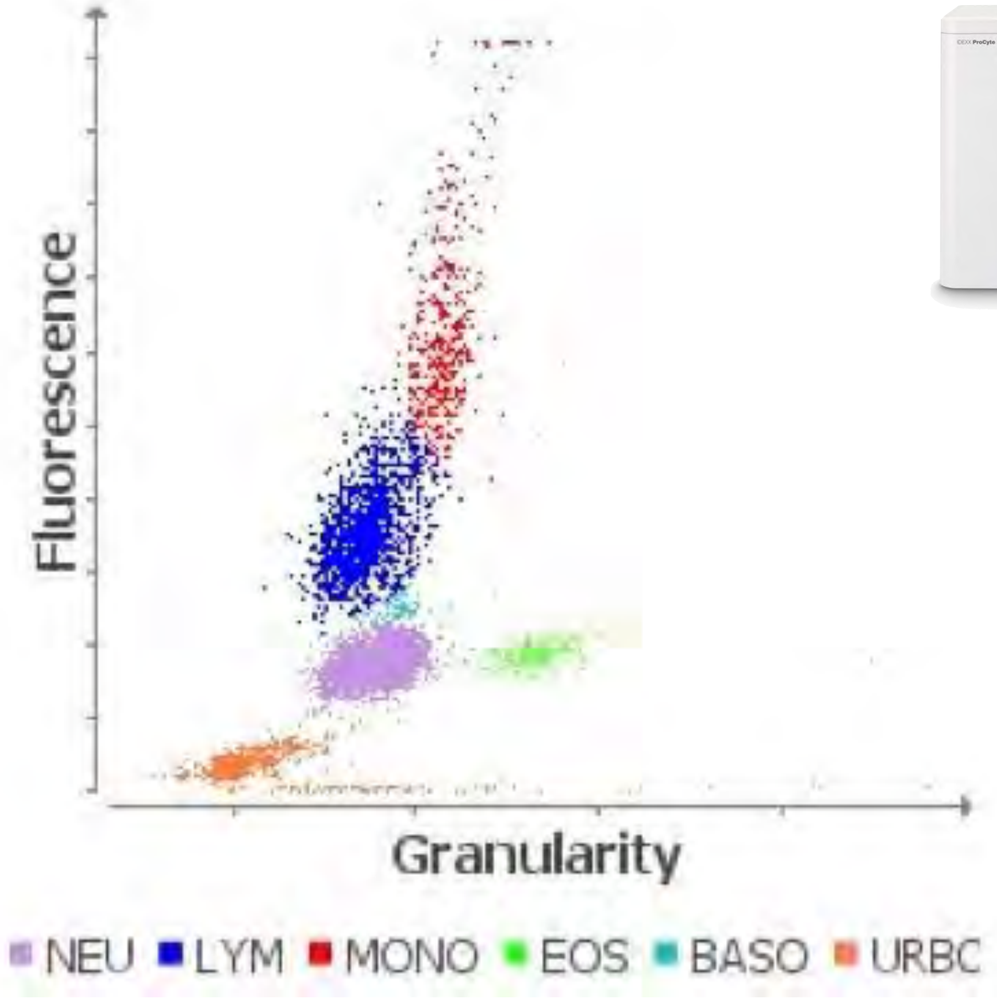


Acute









CLL/Indolent lymphoma

“Monster”

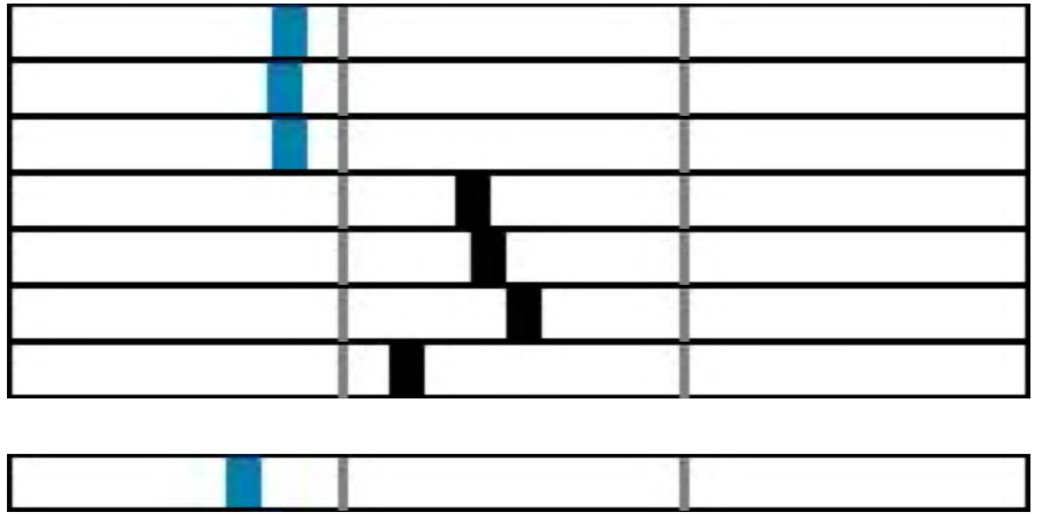
- 3-year-old, MC, Husky cross
- Owned by vet student
- Hypersalivating and panting all night
- PE: cranial abdominal organomegaly

"Monster"

Client: [redacted]
Patient Name: monster
Species: Canine
Breed:

Gender:
Weight: 0.0 lbs
Age:
Doctor:

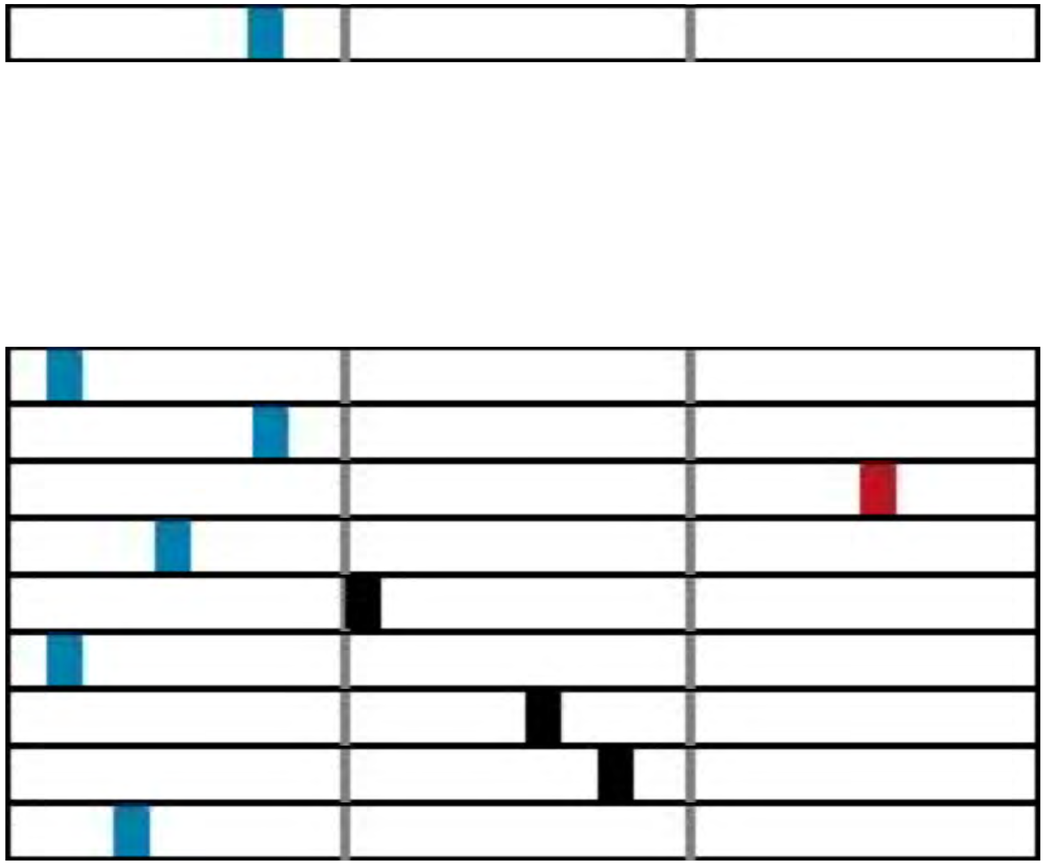
Test	Results	Reference Interval	LOW	NORMAL	HIGH
ProCyte Dx (December 26, 2012 11:03 AM)					
RBC	5.13 M/µL	5.65 - 8.87	LOW		
HCT	33.9 %	37.3 - 61.7	LOW		
HGB	11.9 g/dL	13.1 - 20.5	LOW		
MCV	66.1 fL	61.6 - 73.5			
MCH	23.2 pg	21.2 - 25.9			
MCHC	35.1 g/dL	32.0 - 37.9			
RDW	15.1 %	13.6 - 21.7			
%RETIC	0.1 %				
RETIC	7.2 K/µL	10.0 - 110.0	LOW		



IDEXX

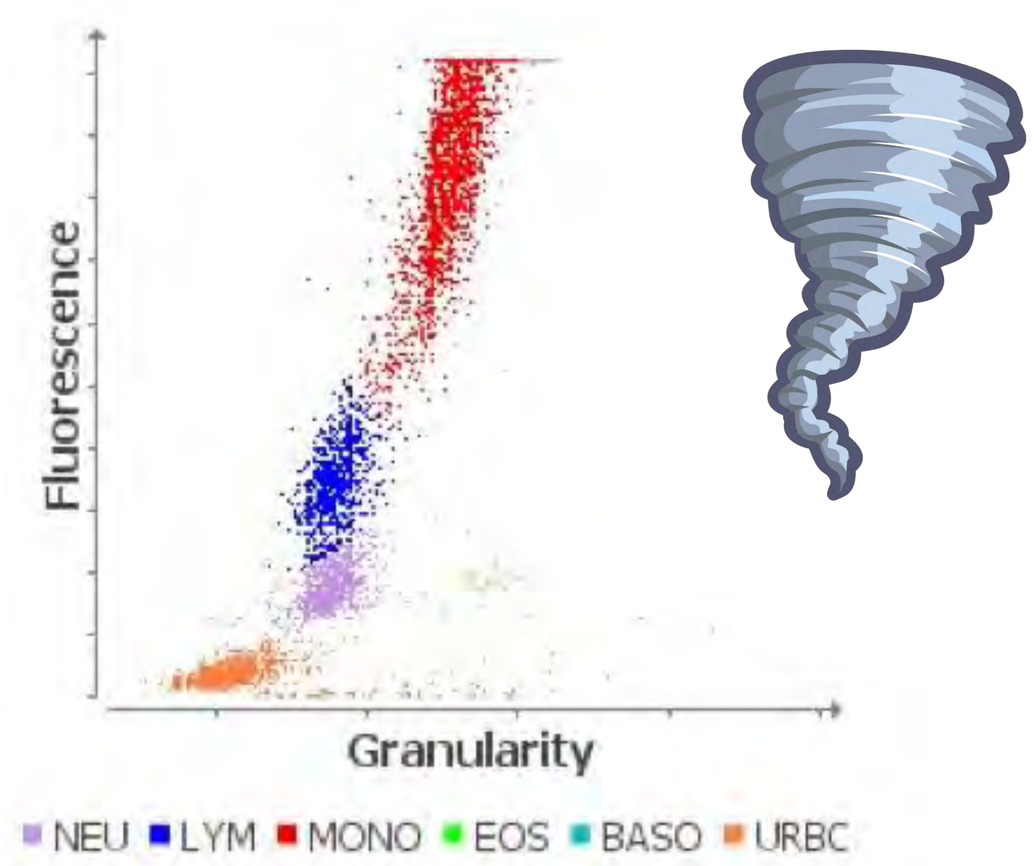
“Monster”

WBC	4.36 K/µL	5.05 - 16.76	LOW
%NEU	22.0 %		
%LYM	19.5 %		
%MONO	57.8 %		
%EOS	0.7 %		
%BASO	0.0 %		
NEU	0.96 K/µL	2.95 - 11.64	LOW
LYM	0.85 K/µL	1.05 - 5.10	LOW
MONO	2.52 K/µL	0.16 - 1.12	HIGH
EOS	0.03 K/µL	0.06 - 1.23	LOW
BASO	0.00 K/µL	0.00 - 0.10	
PLT	49 K/µL	148 - 484	LOW
MPV	11.3 fL	8.7 - 13.2	
PDW	17.2 fL	9.1 - 19.4	
PCT	0.06 %	0.14 - 0.46	LOW



"Monster"

"Monster"



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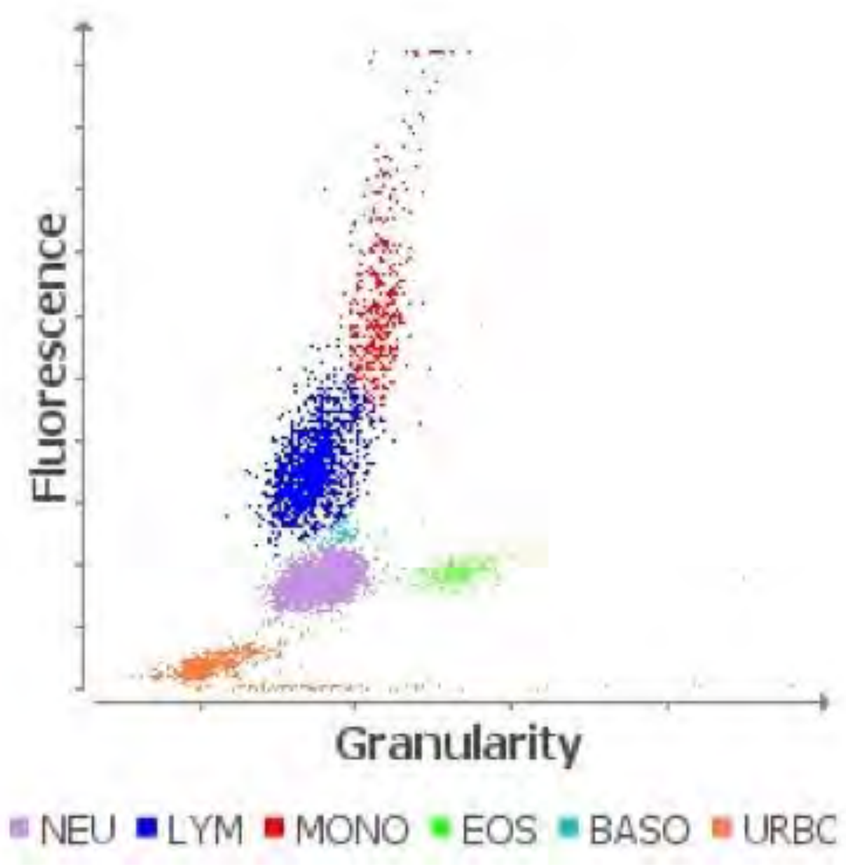
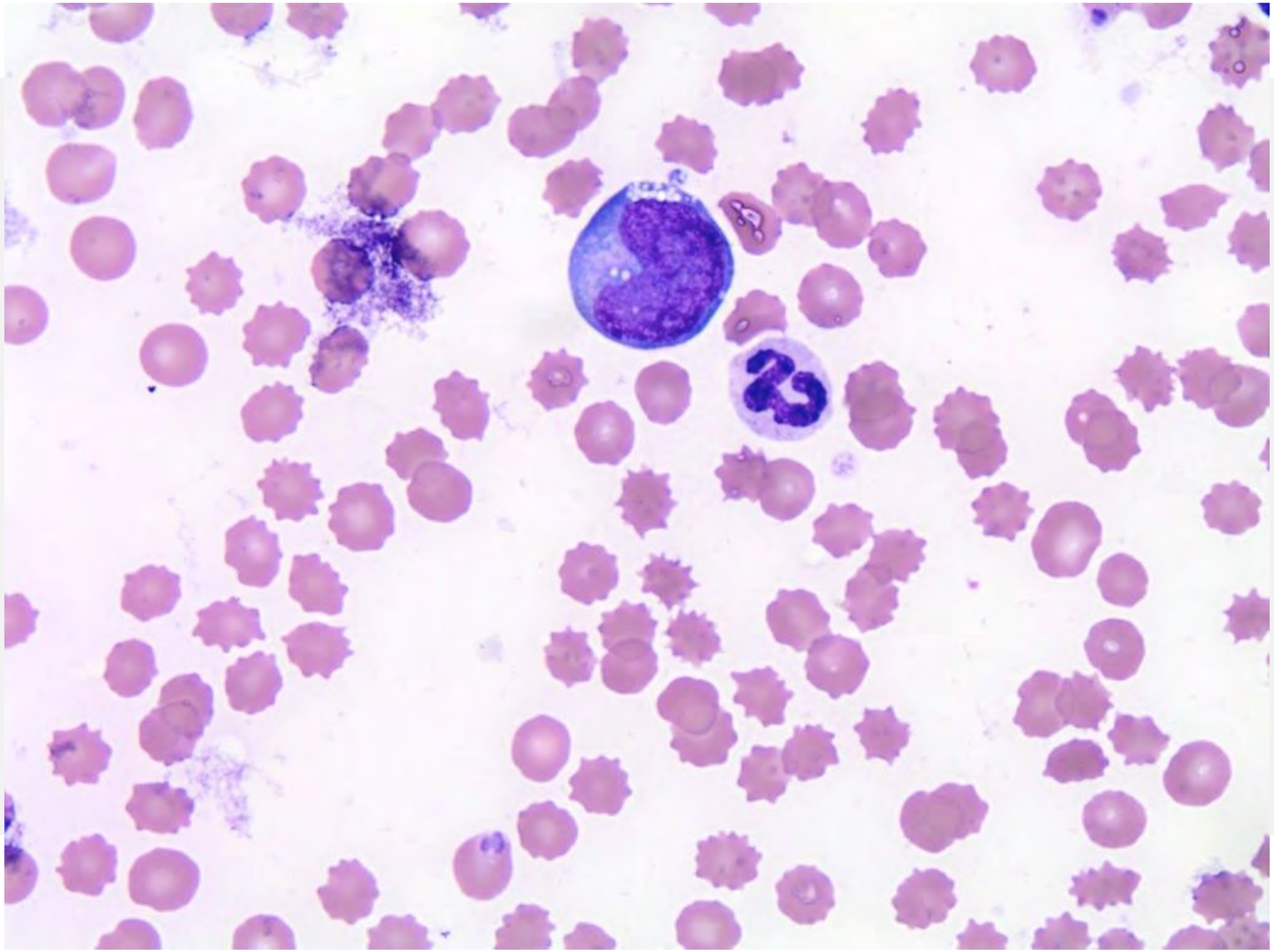
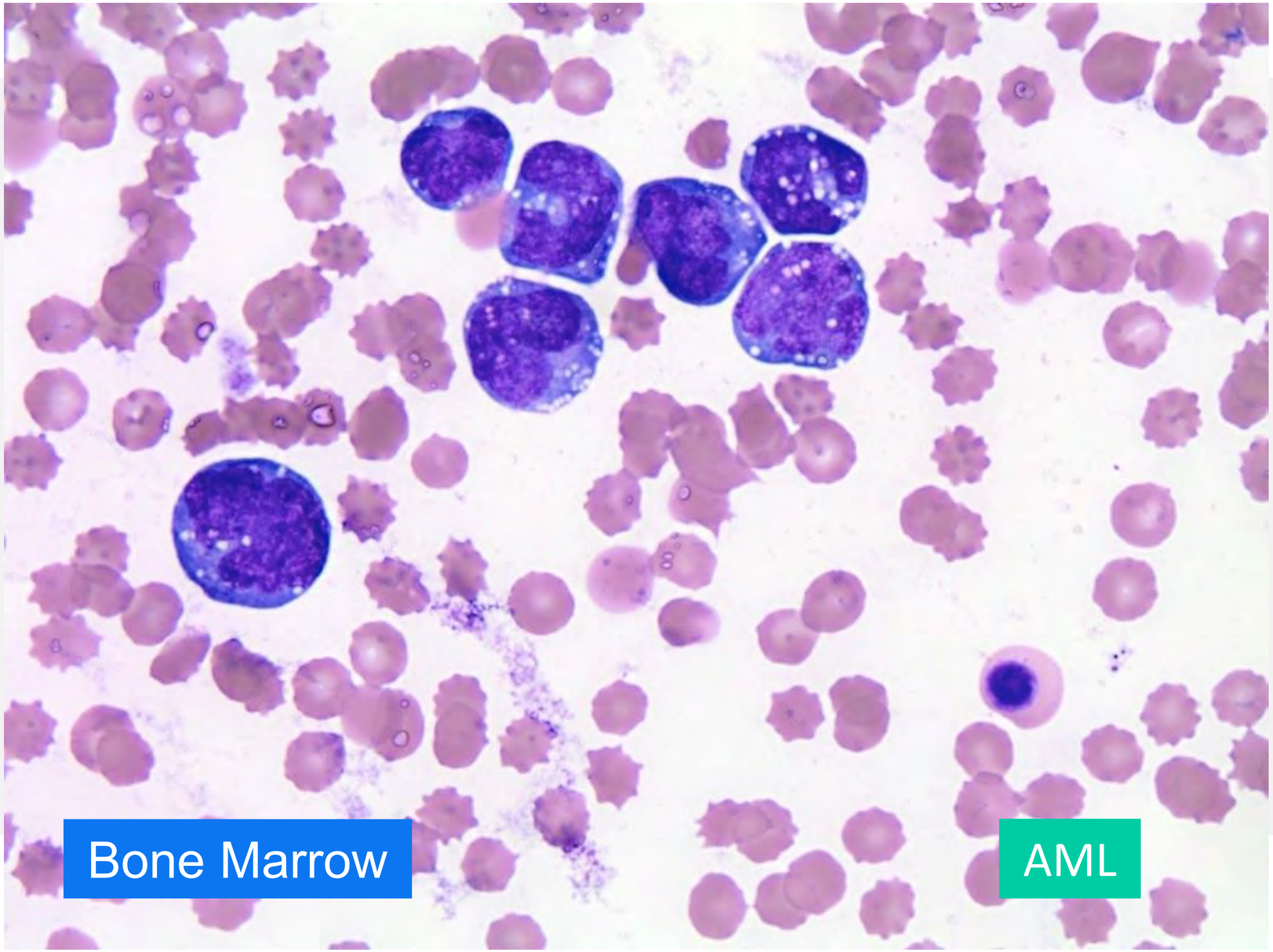






CBC in Oncology

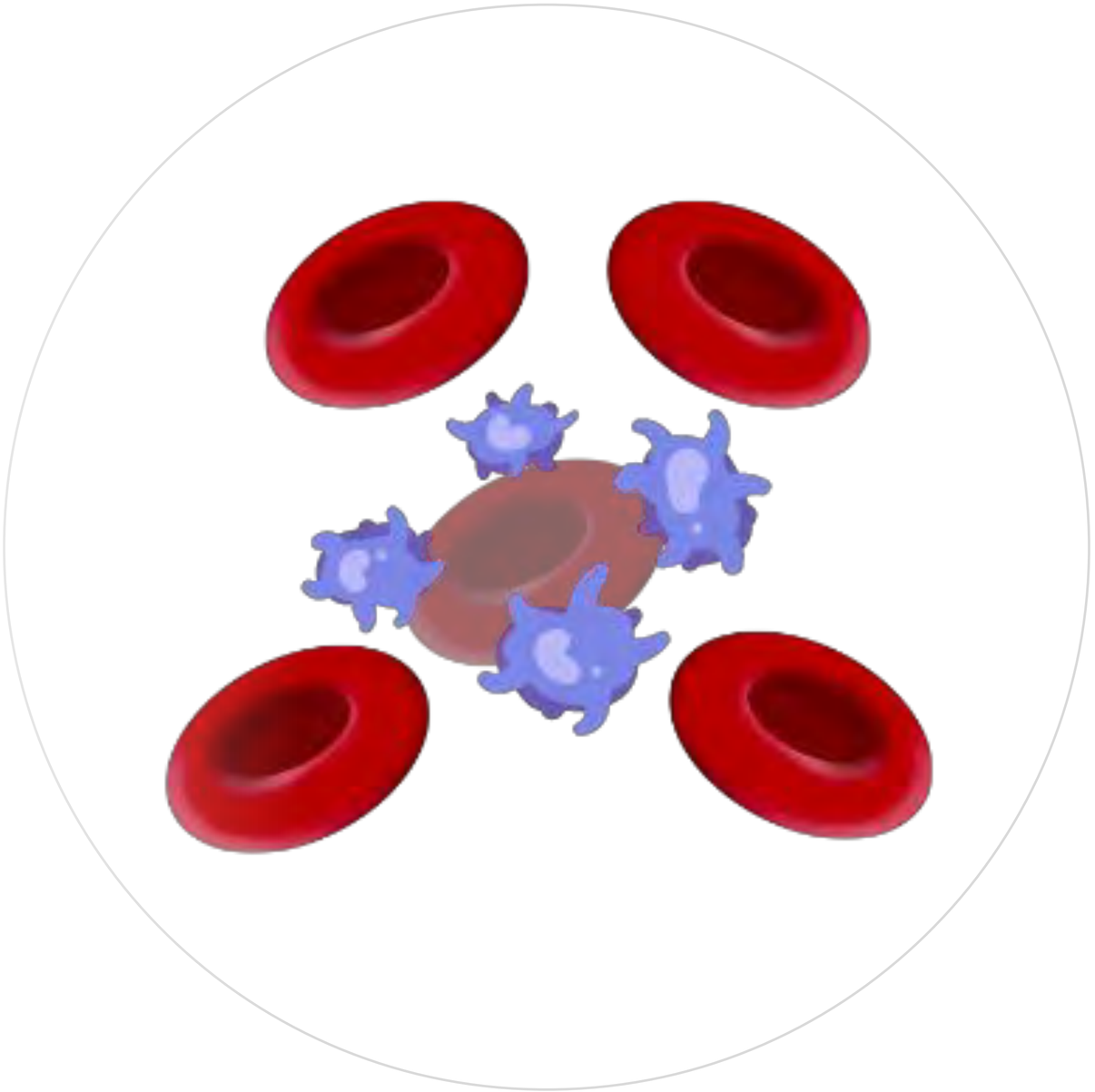
Platelets/hemostasis

01 Thrombocytopenia

02 Thrombocytosis

03 Bleeding

04 Thrombosis



CBC in Oncology

Platelets

- **Thrombocytopenia**
  - 1/3 cancer patients
    - Leukemias
    - Lymphoma
    - Myeloma
    - HSA
    - MH

All “thrombocytopenias”
should have a blood smear or cytogram review

CBC in Oncology

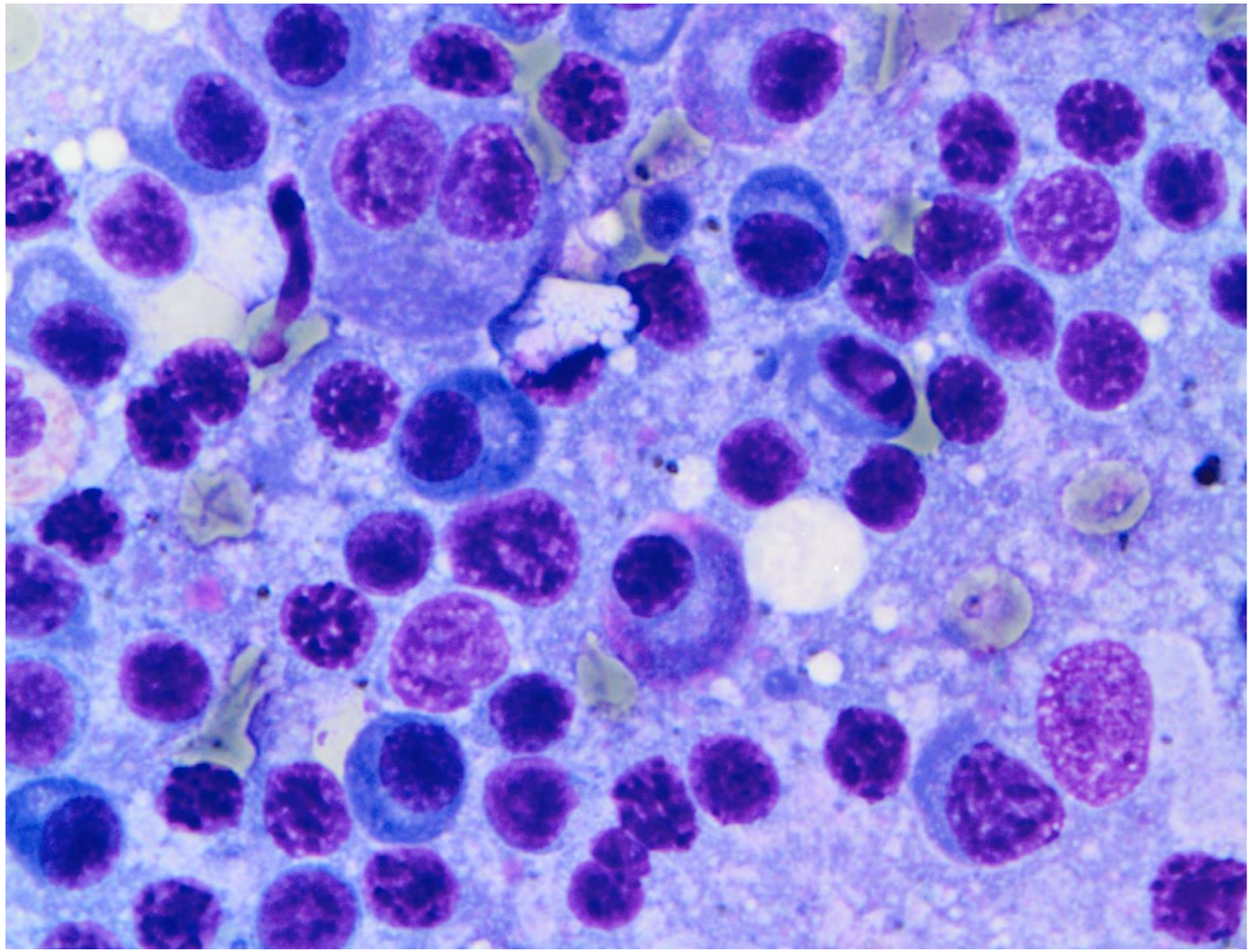
Platelets

- **Thrombocytosis**
  - 1/3 dogs with thrombocytosis have cancer
  - 50% of dogs w/carcinoma
  - Essential thrombocythemia
  - Clinically relevant?

CBC in Oncology

Bi- or Pancytopenia

+Leukemia
+Lymphoma
+Myeloma
+MH (hemophagocytic)



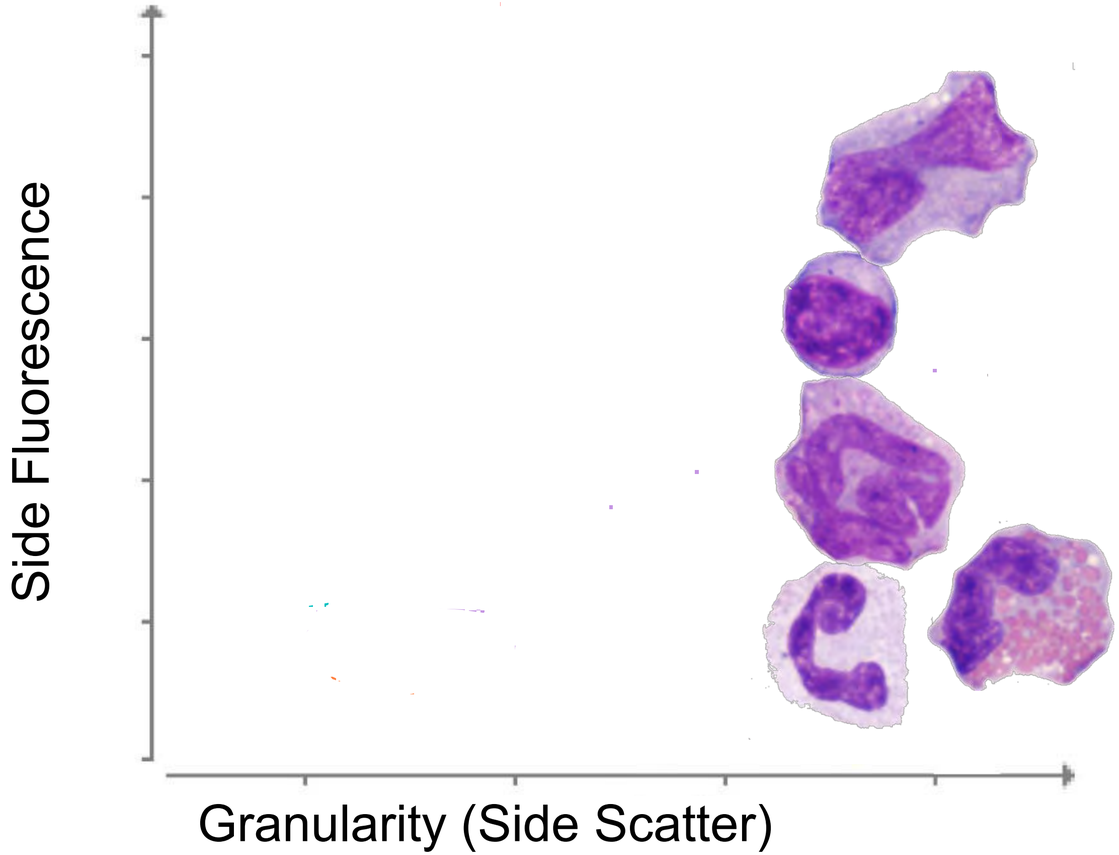
Let The Dotplots Tell A Story

“Pudge”

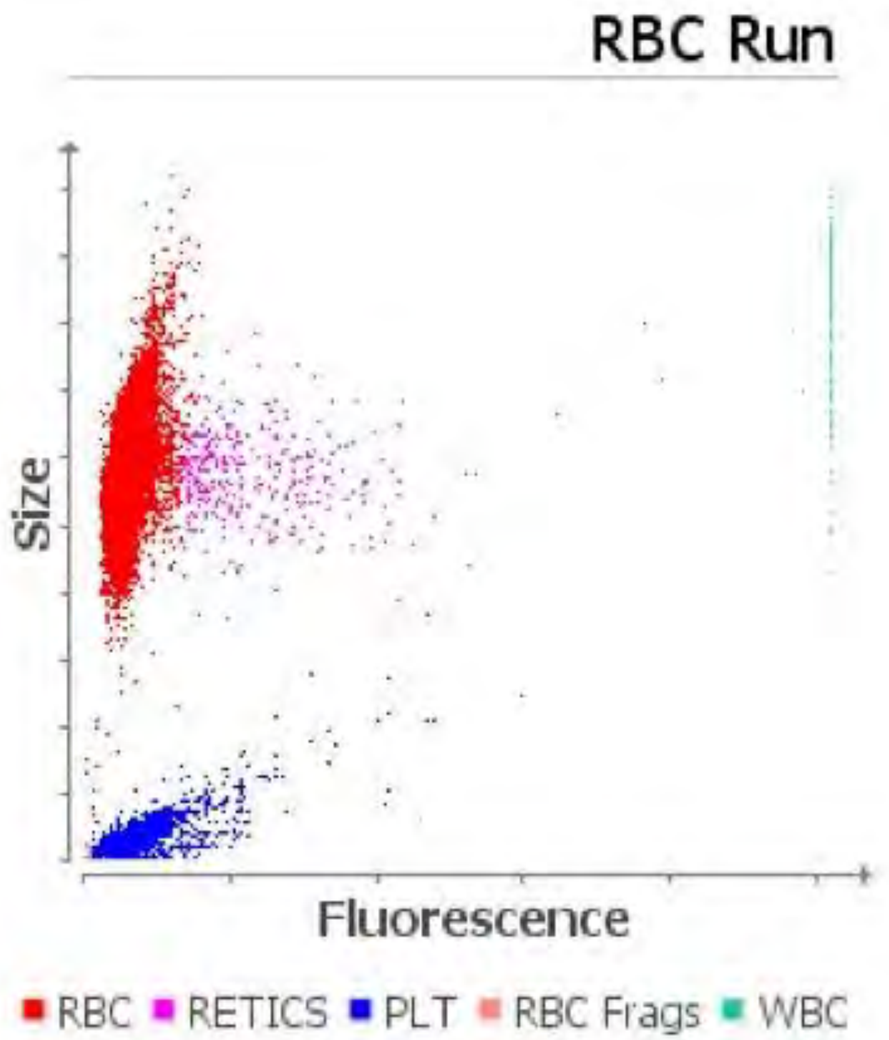
13-year-old, MC, Shepherd mix with multicentric lymphoma on CHOP

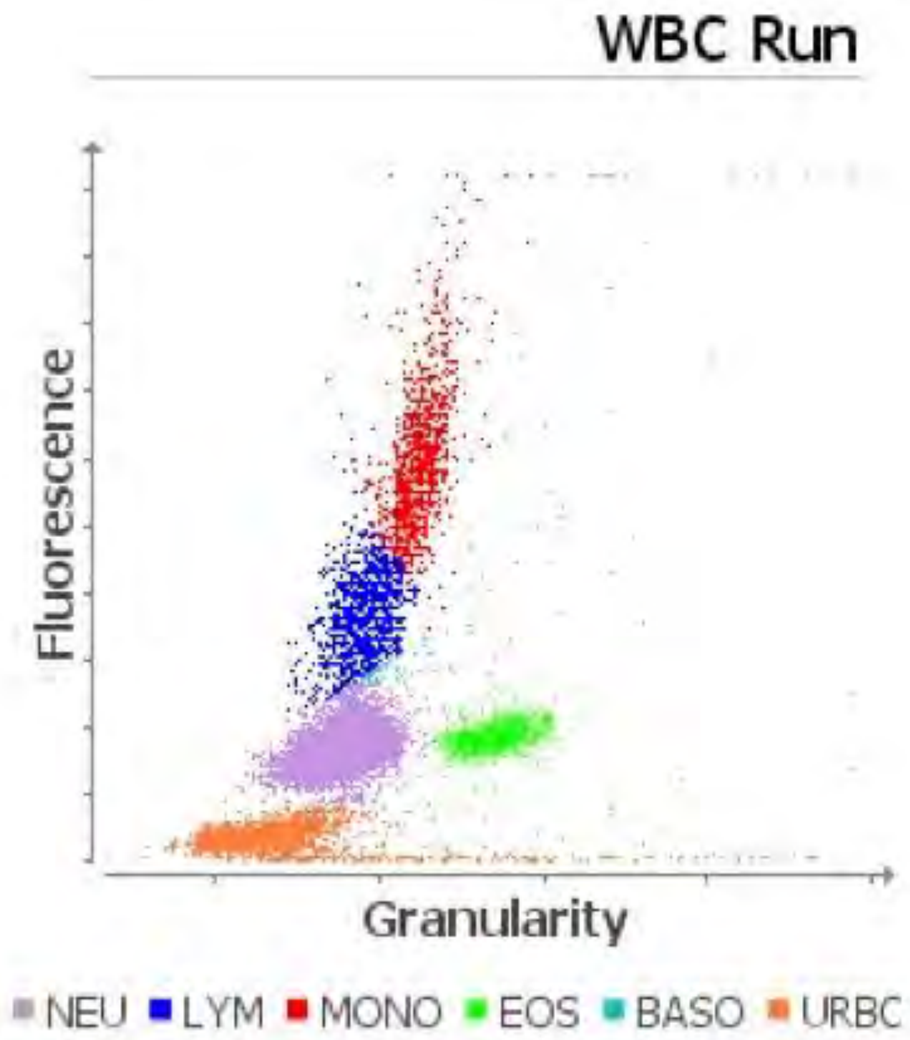
-

CBC: WBC Dot Plot-Refresher

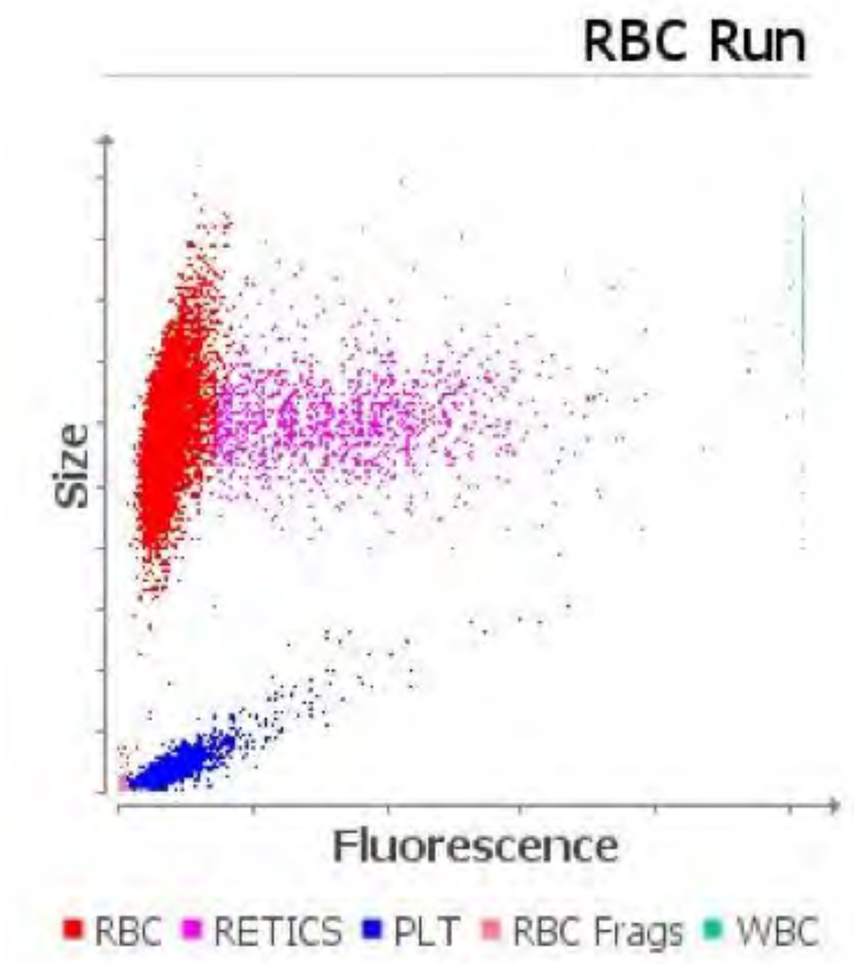


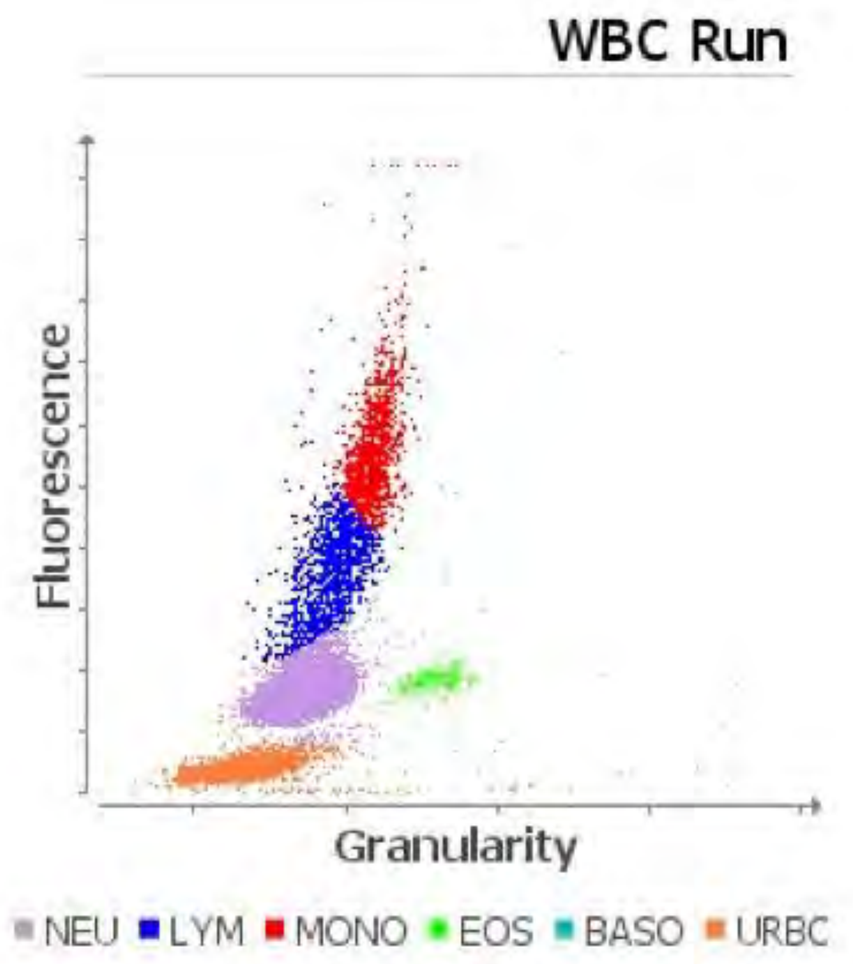
Day 1


RBC Run
Size
Fluorescence
RBC
RETICS
PLT
RBC Frags
WBC

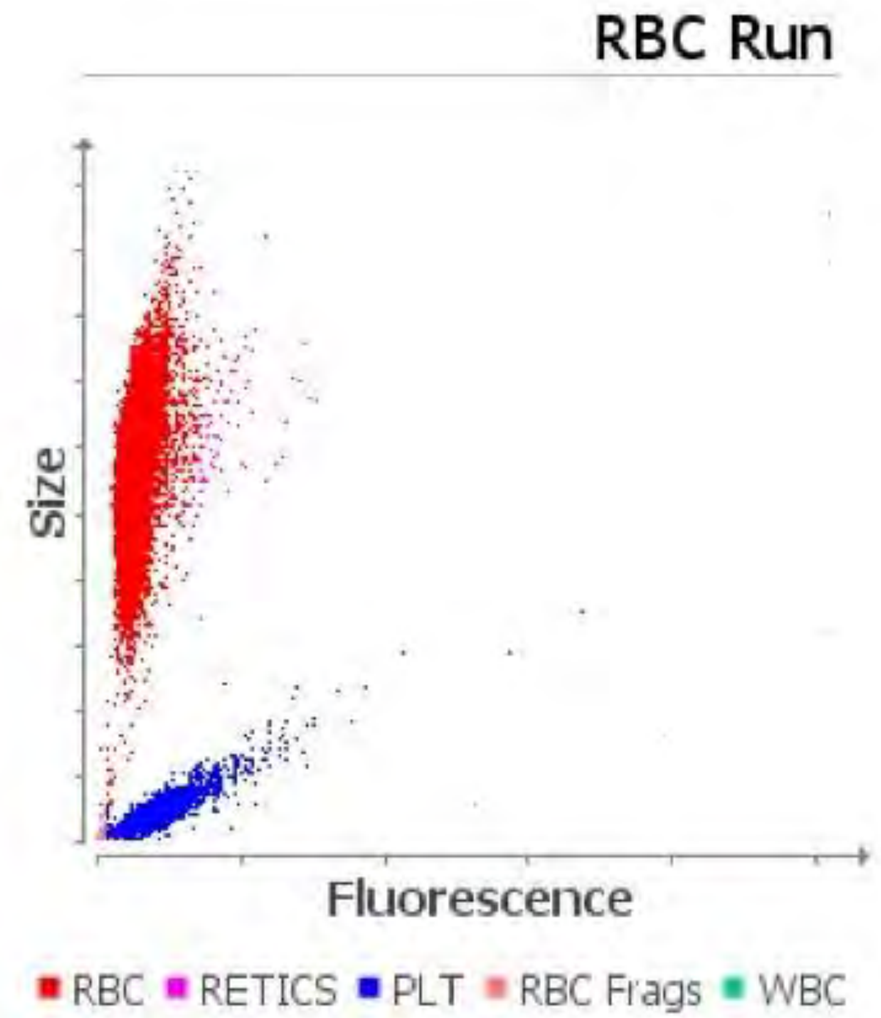

WBC Run
Fluorescence
Granularity
NEU
LYM
MONO
EOS
BASO
URBC

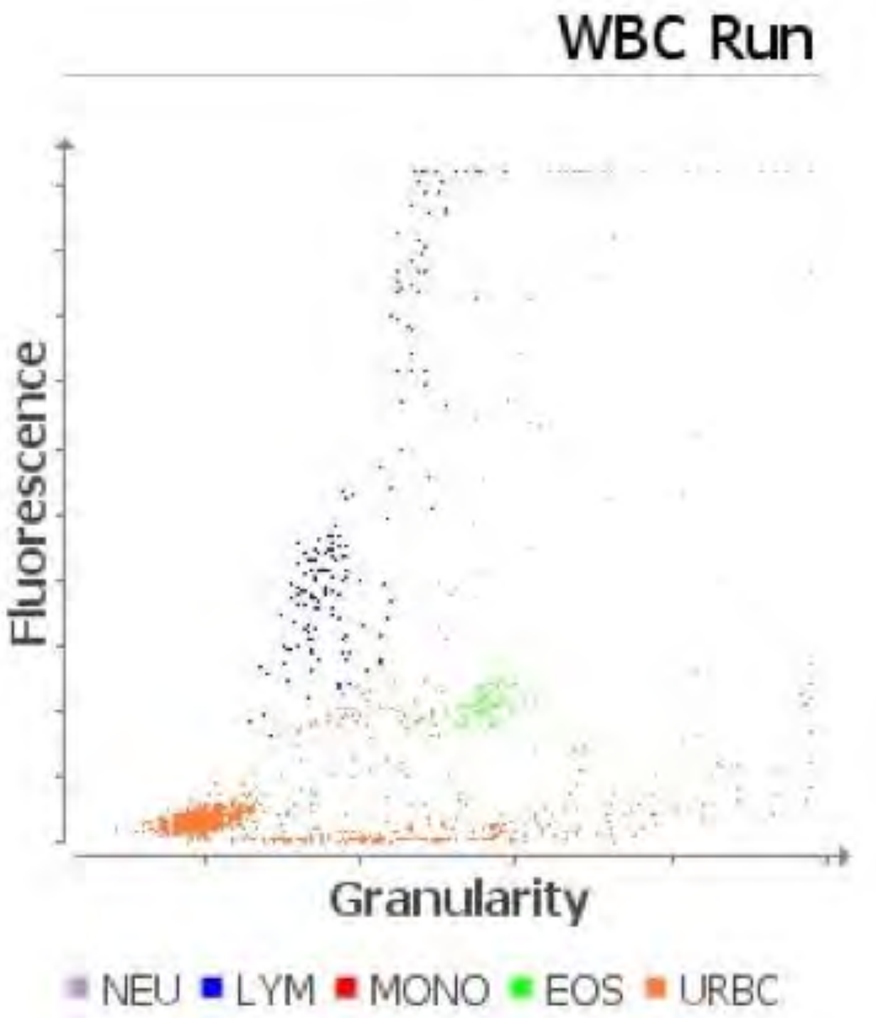
Day 8


RBC Run
Size
Fluorescence
RBC
RETICS
PLT
RBC Frags
WBC

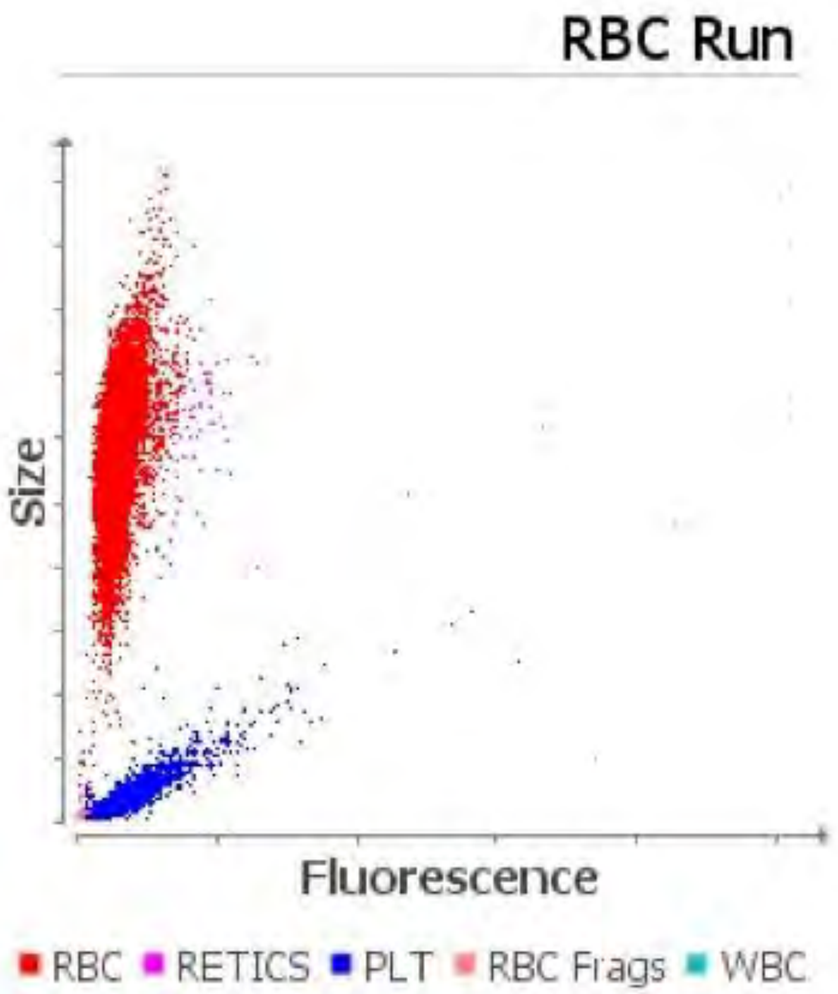

WBC Run
Fluorescence
Granularity
NEU
LYM
MONO
EOS
BASO
URBC

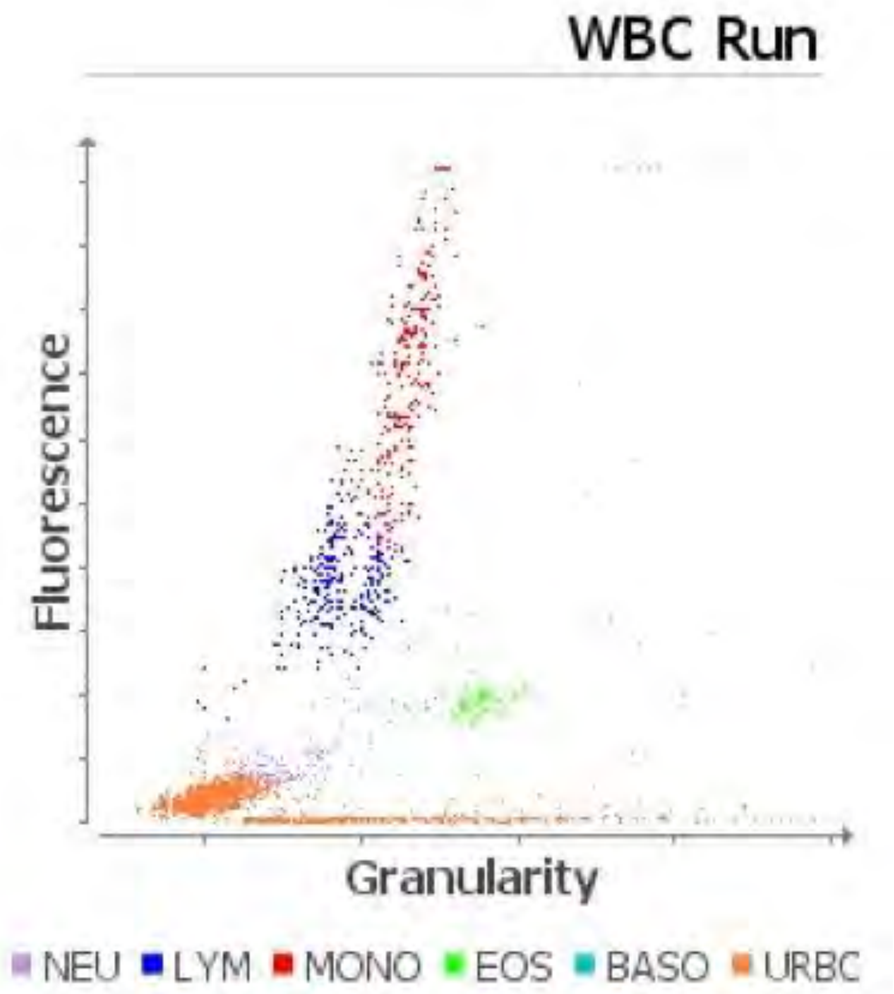
Day 30


RBC Run
Size
Fluorescence
RBC
RETICS
PLT
RBC Frags
WBC

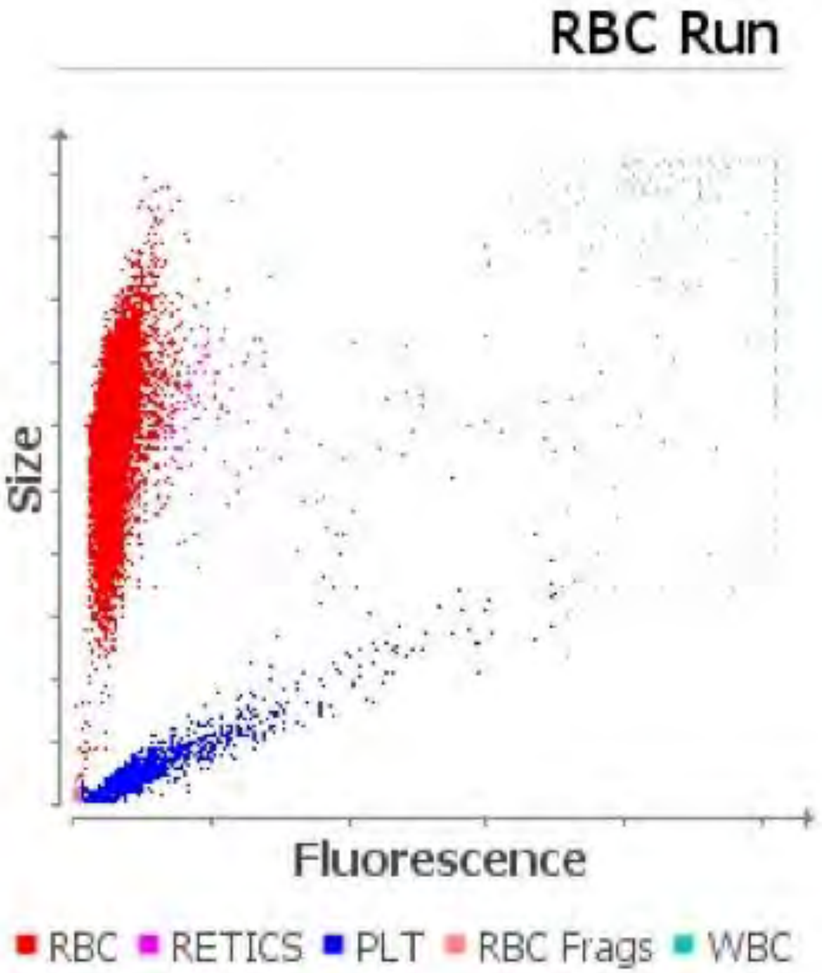

WBC Run
Fluorescence
Granularity
NEU
LYM
MONO
EOS
URBC

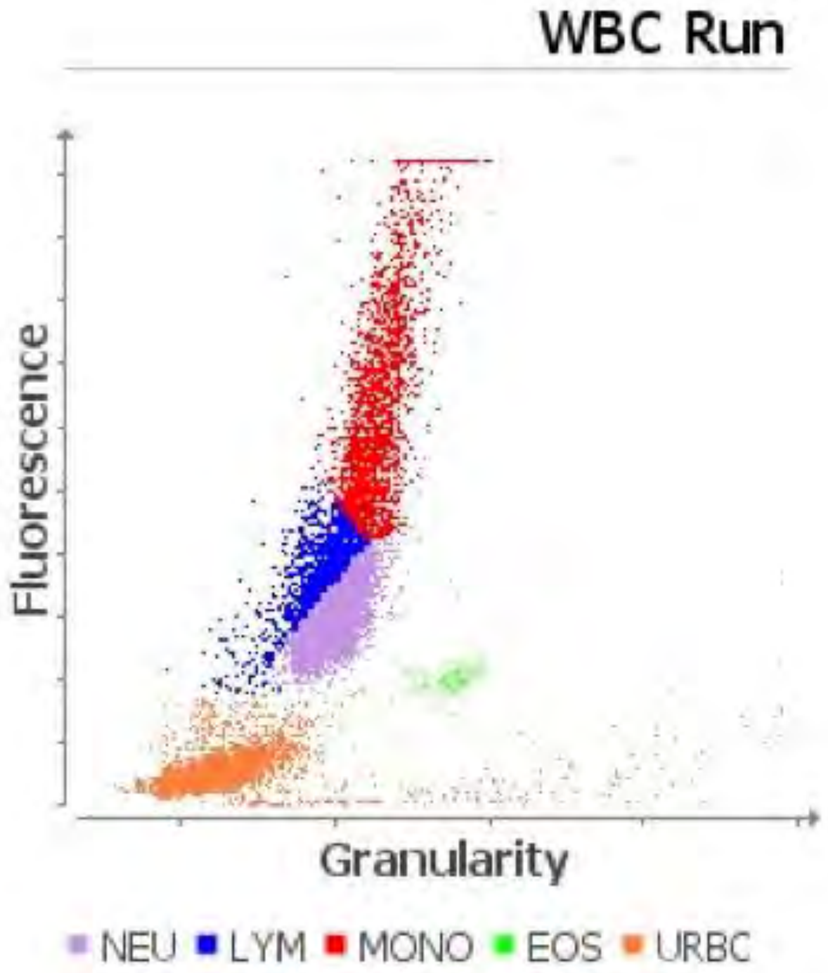
Day 31


RBC Run
Size
Fluorescence
RBC
RETICS
PLT
RBC Frags
WBC

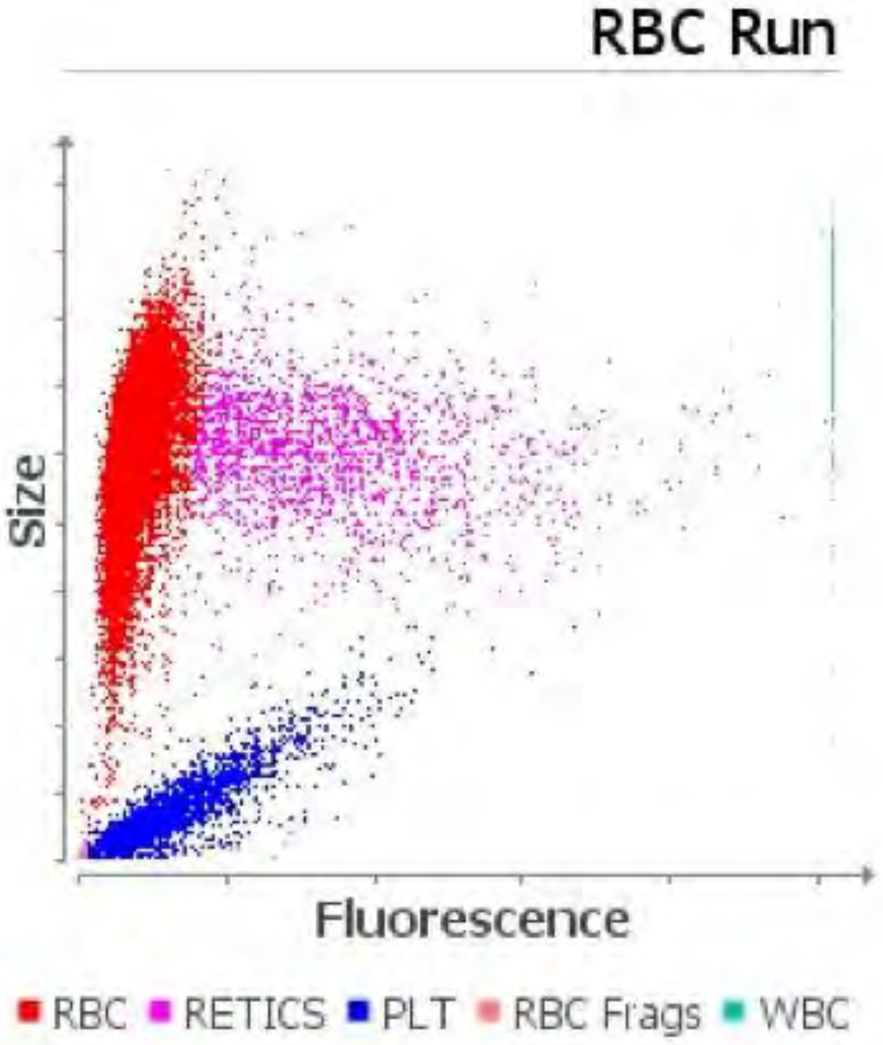

WBC Run
Fluorescence
Granularity
NEU
LYM
MONO
EOS
BASO
URBC

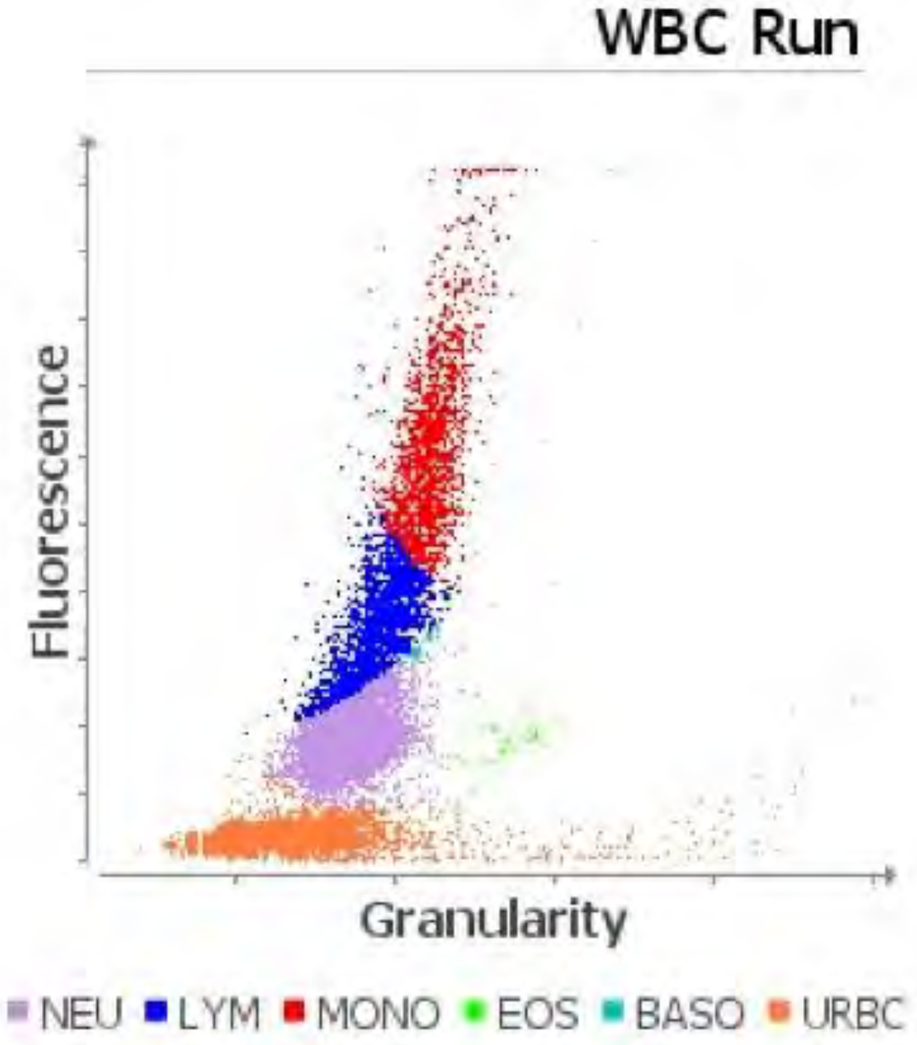
Day 32


RBC Run
Size
Fluorescence
RBC
RETICS
PLT
RBC Frags
WBC

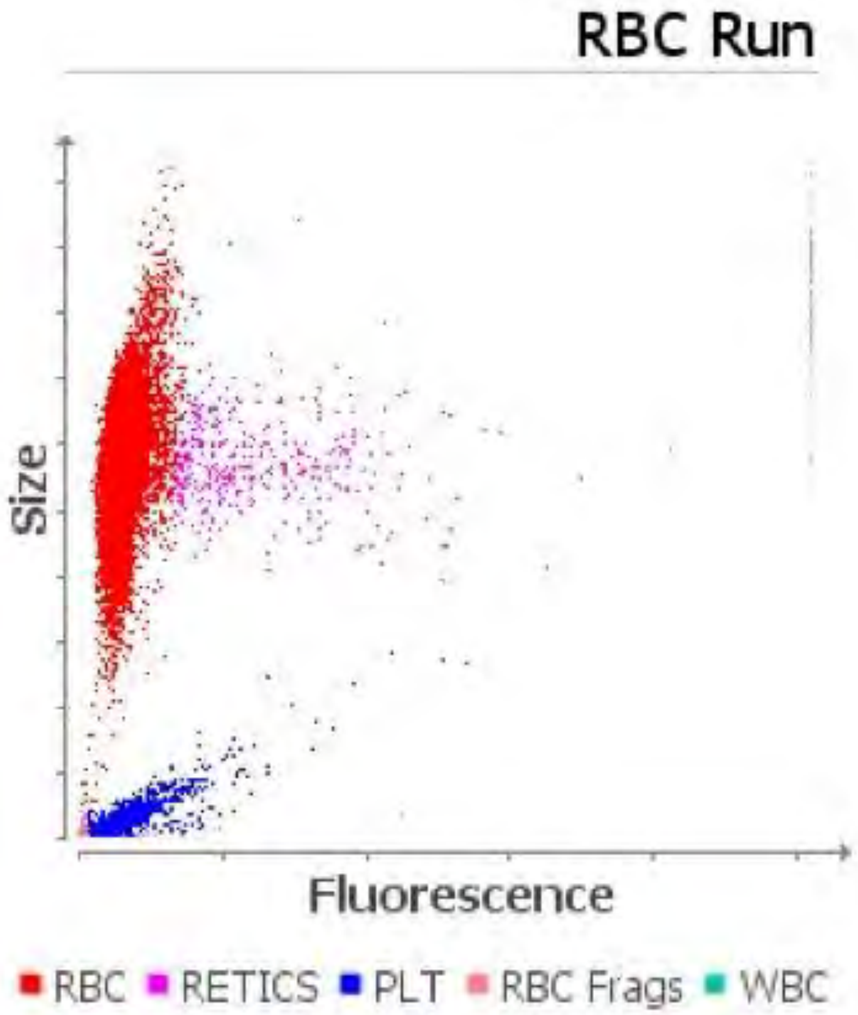

WBC Run
Fluorescence
Granularity
NEU
LYM
MONO
EOS
URBC

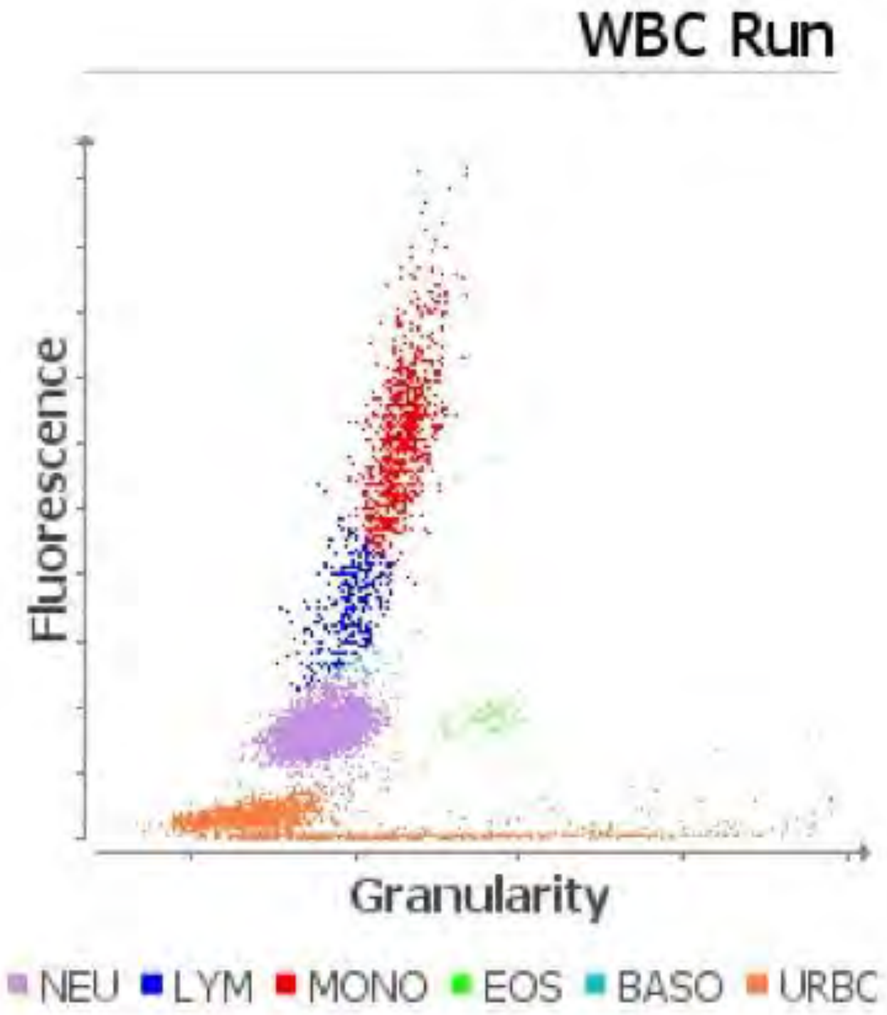
Day 38


RBC Run
Size
Fluorescence
RBC
RETICS
PLT
RBC Frags
WBC

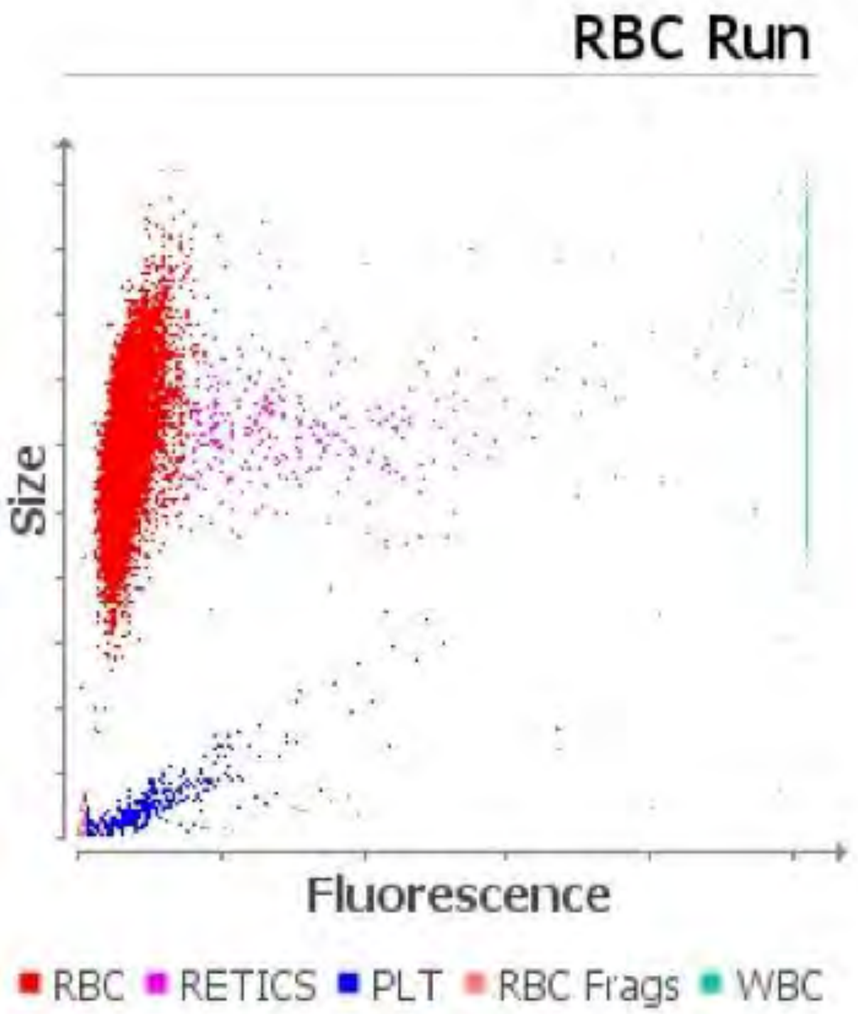

WBC Run
Fluorescence
Granularity
NEU
LYM
MONO
EOS
BASO
URBC

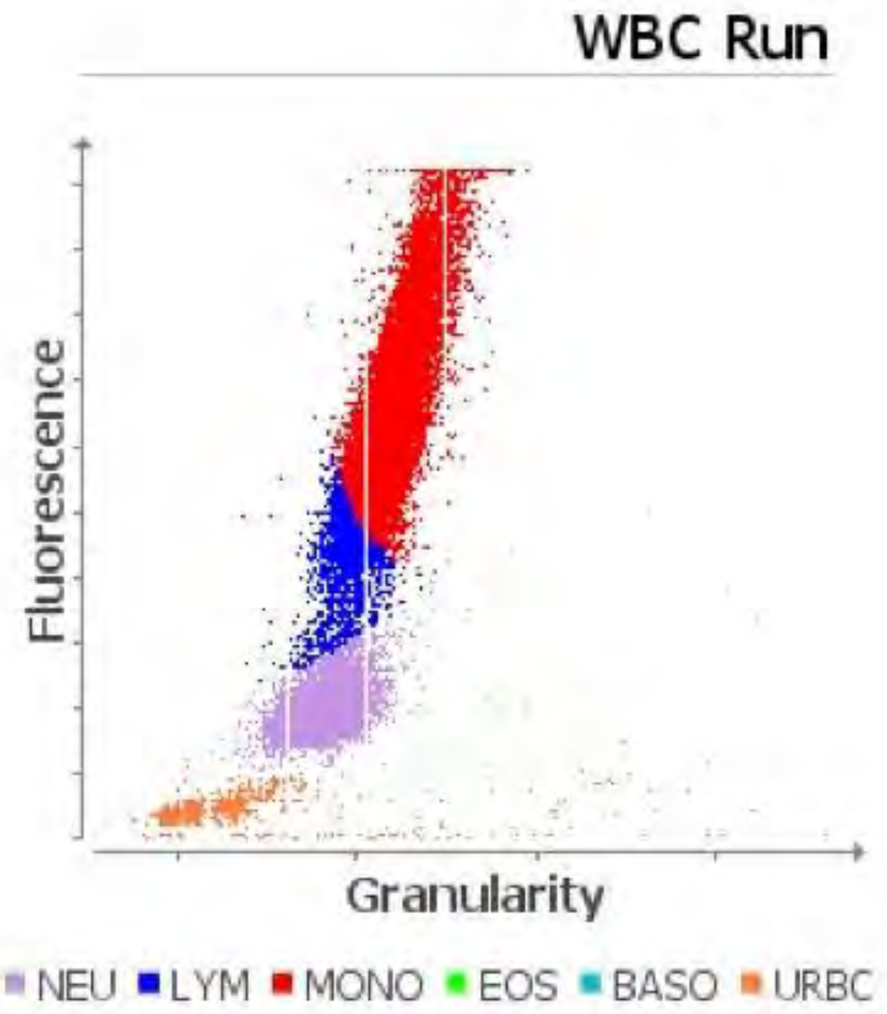
Day 86


RBC Run
Size
Fluorescence
RBC
RETICS
PLT
RBC Frags
WBC

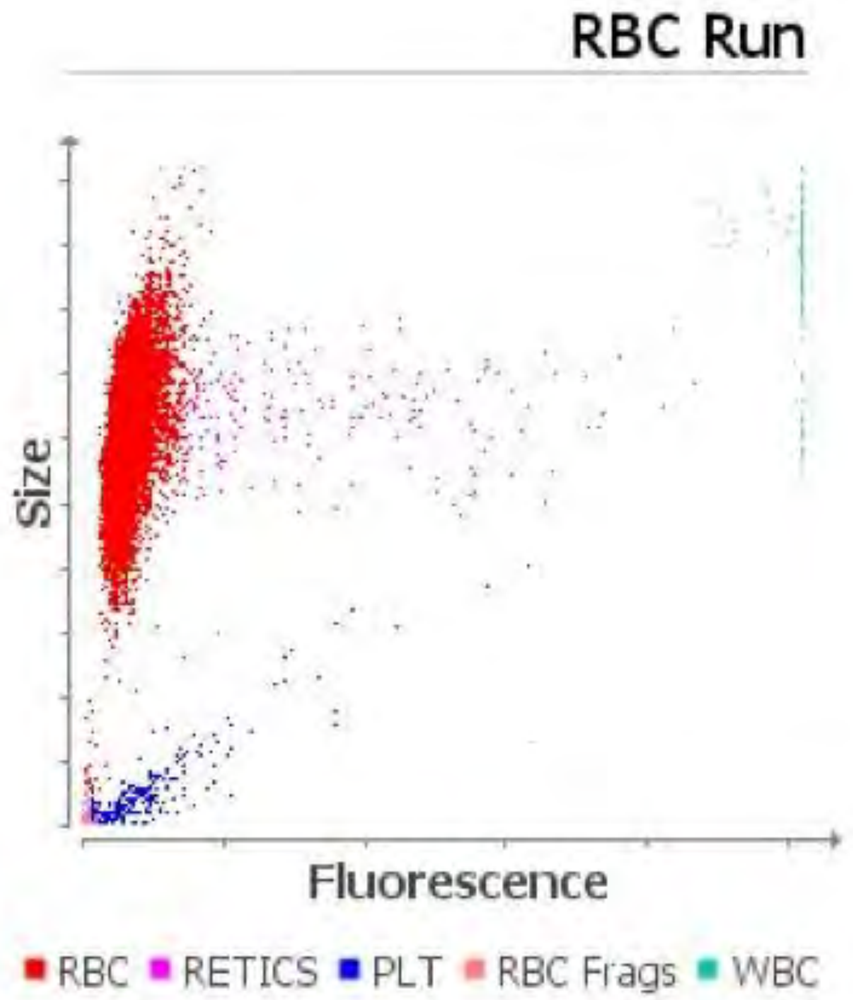

WBC Run
Fluorescence
Granularity
NEU
LYM
MONO
EOS
BASO
URBC

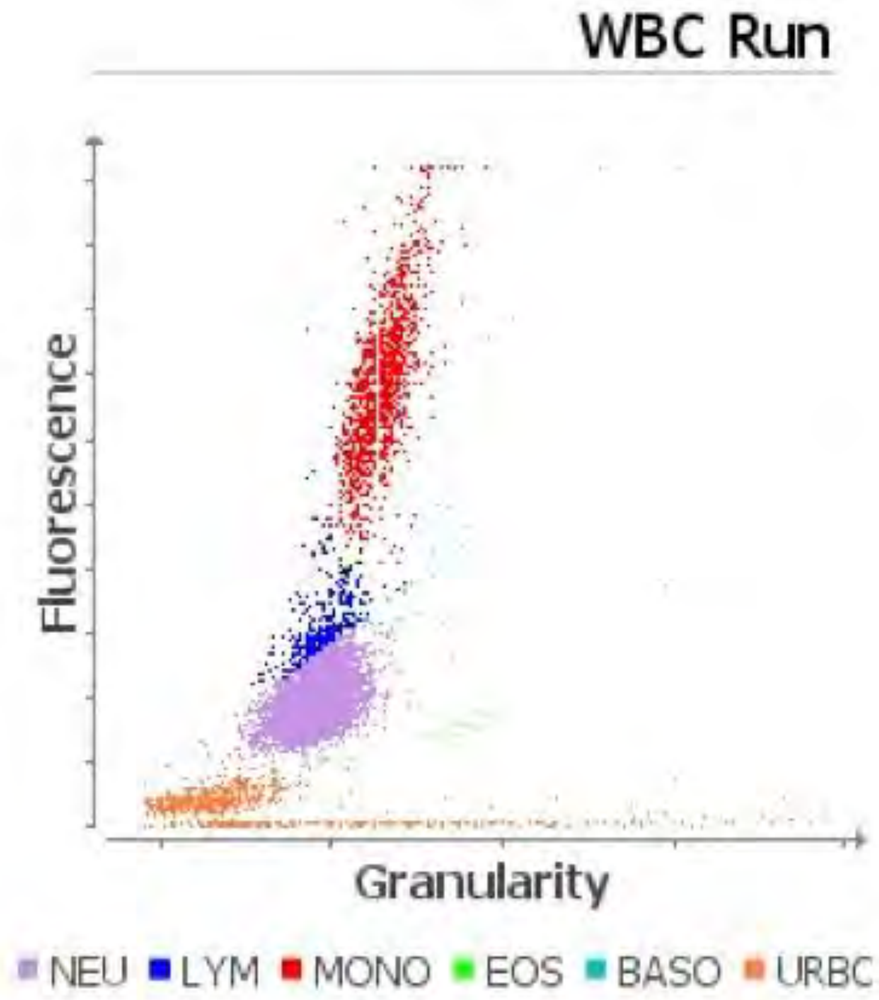
Day 150


RBC Run
Size
Fluorescence
RBC
RETICS
PLT
RBC Frags
WBC

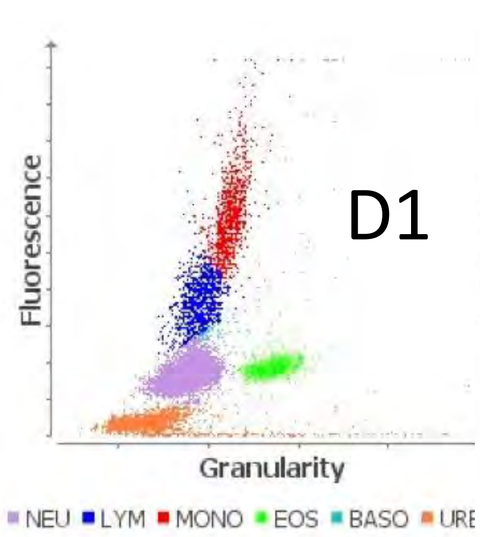

WBC Run
Fluorescence
Granularity
NEU
LYM
MONO
EOS
BASO
URBC

Day 156

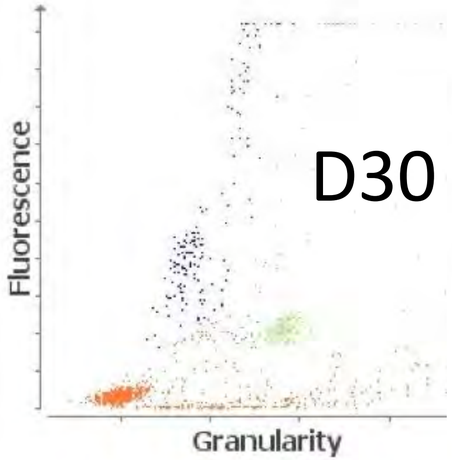

RBC Run
Size
Fluorescence
RBC
RETICS
PLT
RBC Frags
WBC


WBC Run
Fluorescence
Granularity
NEU
LYM
MONO
EOS
BASO
URBC

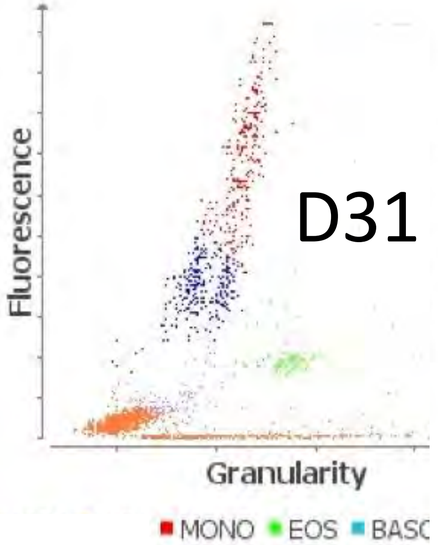
"Pudge"-Sequential WBC



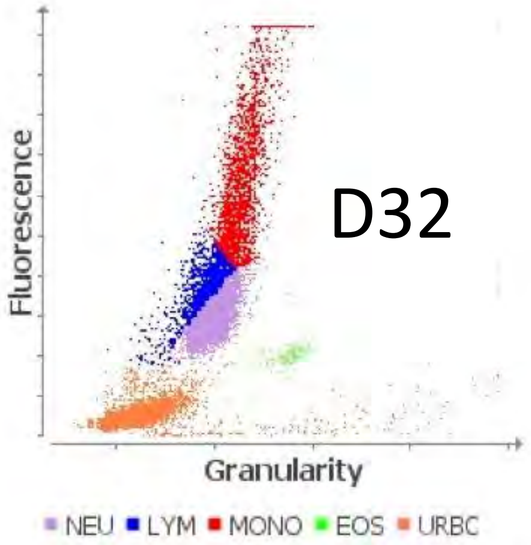
D1



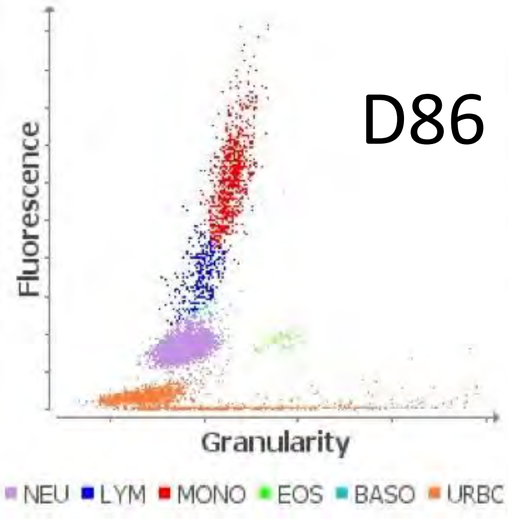
D30



D31



D32



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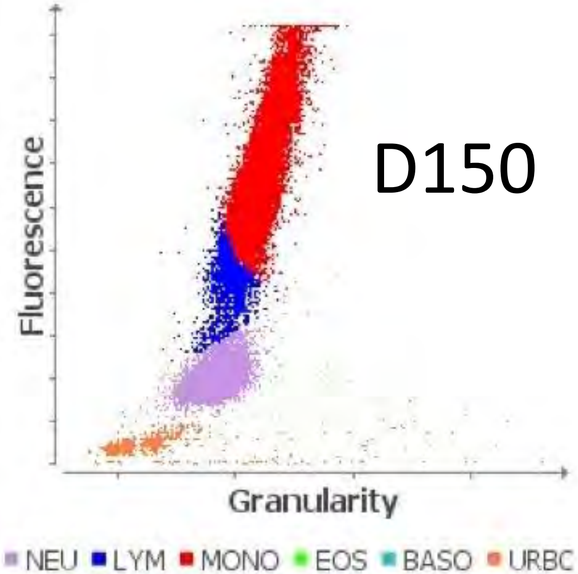
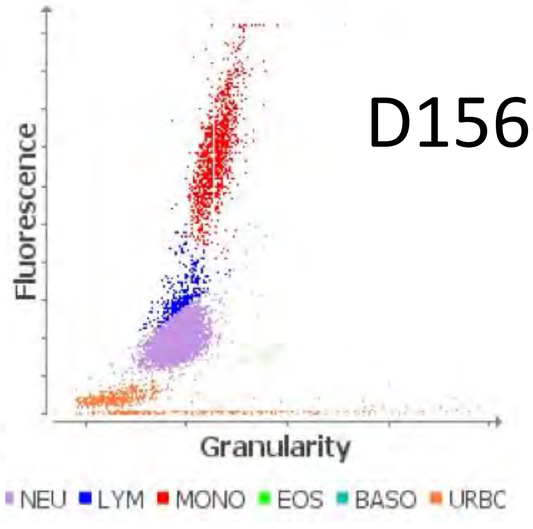
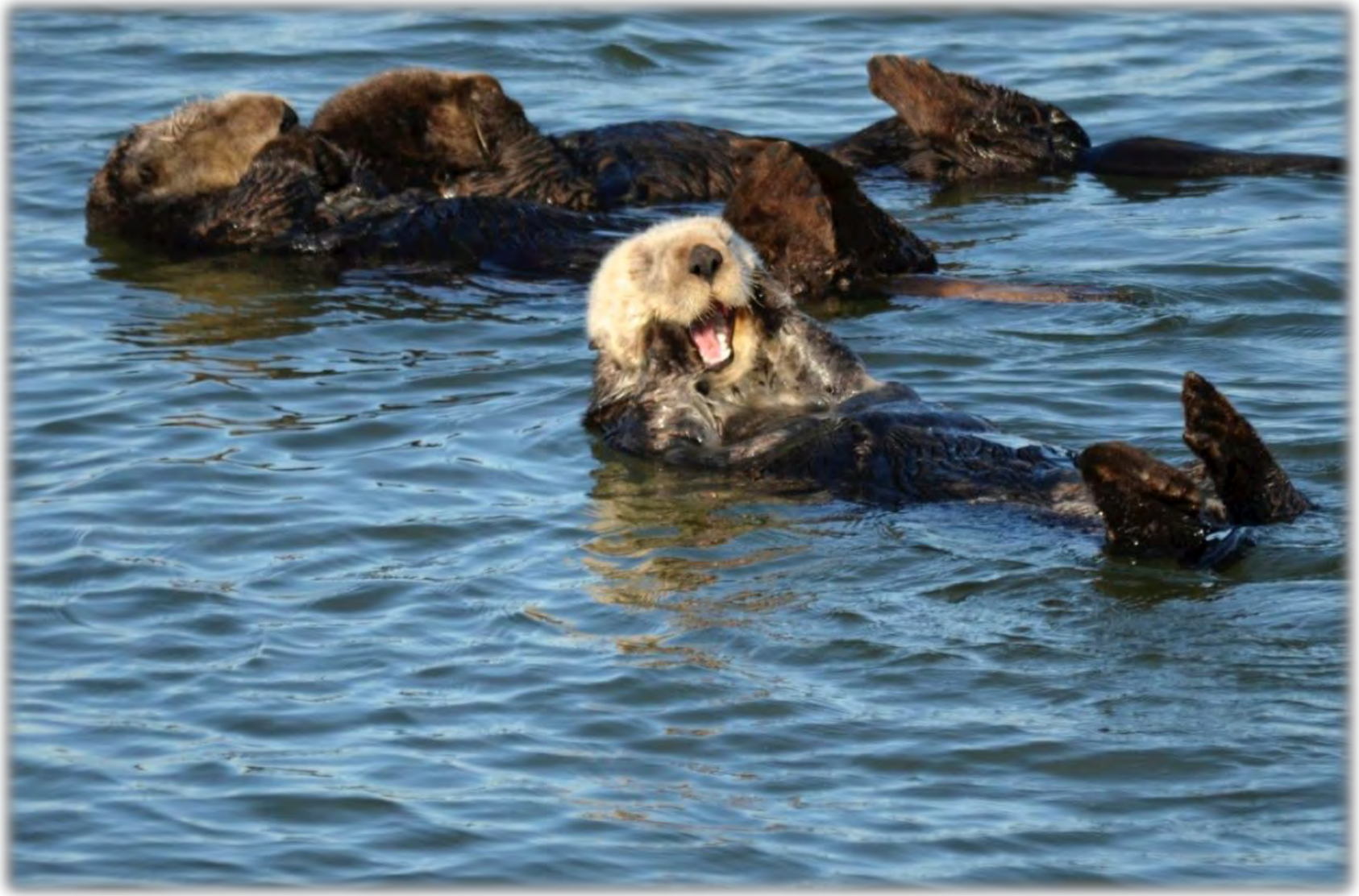


D150



D156

Questions?



"Simon", 9, MC, DSH

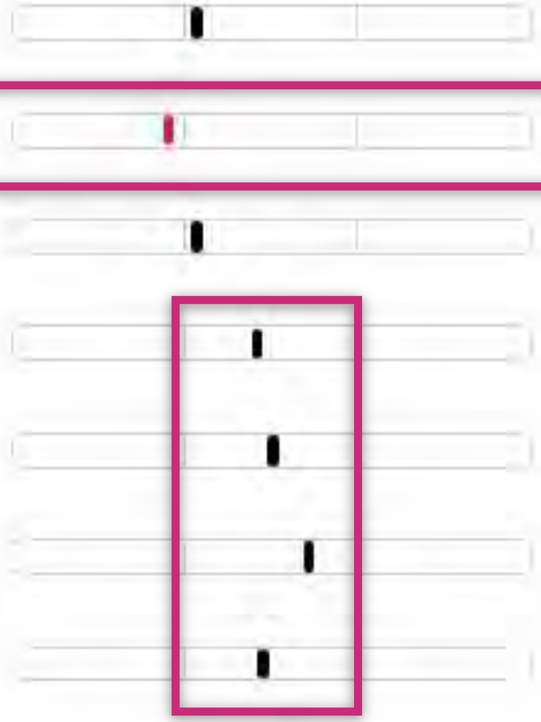
- Referred for hepatic lipidosis

Thanks to Drs. Jason Couto and Kate Sycamore

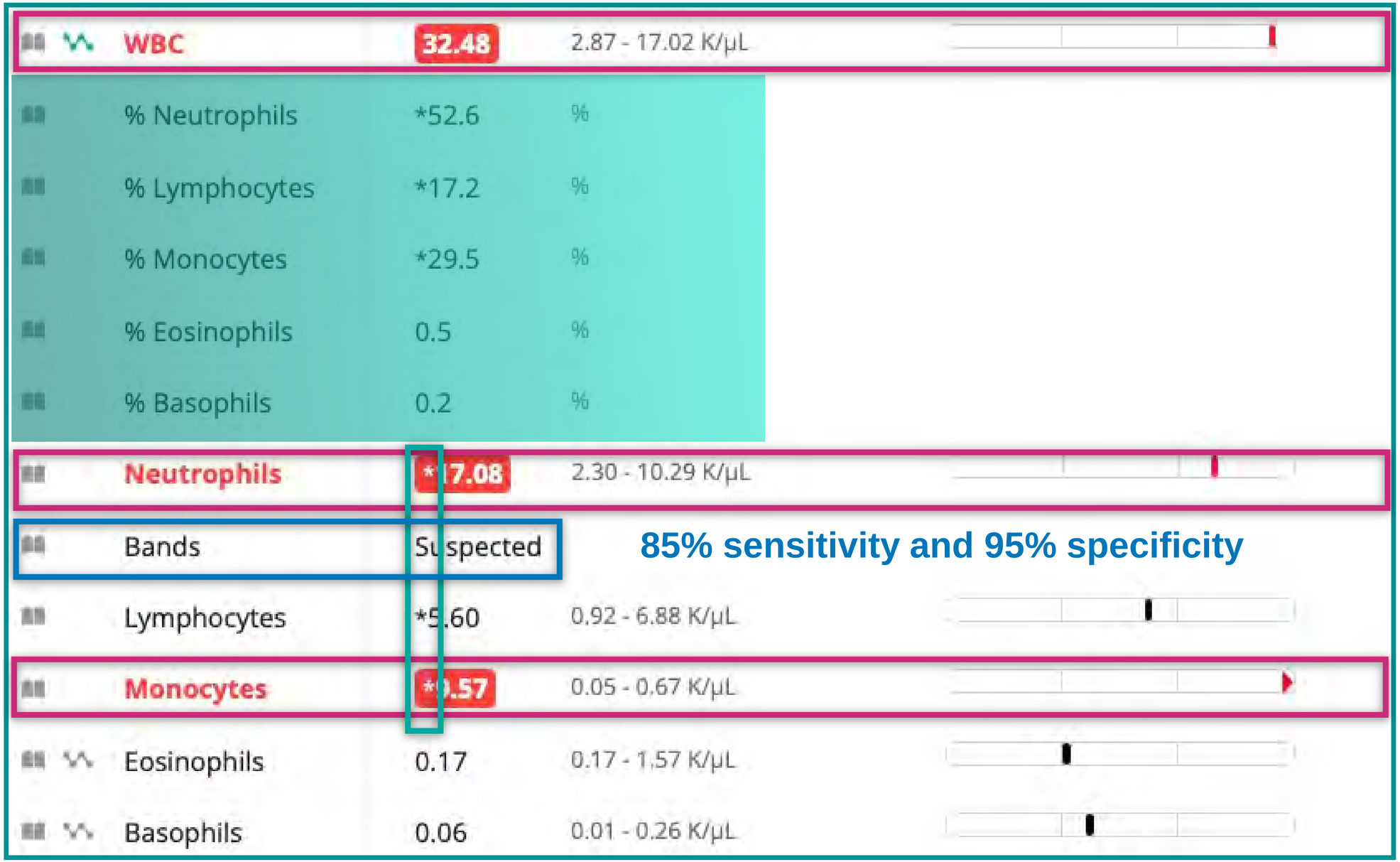
PACIFIC NORTHWEST
PET ER & SPECIALTY CENTER

Simon-CBC-RBCs

RBC	6.75	6.54 - 12.20 M/µL	
Haematocrit	**29.5**	30.3 - 52.3 %	
Haemoglobin	10.0	9.8 - 16.2 g/dL	
MCV	43.7	35.9 - 53.1 fL	
MCH	14.8	11.8 - 17.3 pg	
MCHC	33.9	28.1 - 35.8 g/dL	
RDW	20.8	15.0 - 27.0 %	
% Reticulocyte	0.2	%	
Reticulocytes	10.1	3.0 - 50.0 K/µL	
Reticulocyte Haemoglobin	14.5	13.2 - 20.8 pg	



Simon-CBC-WBCs



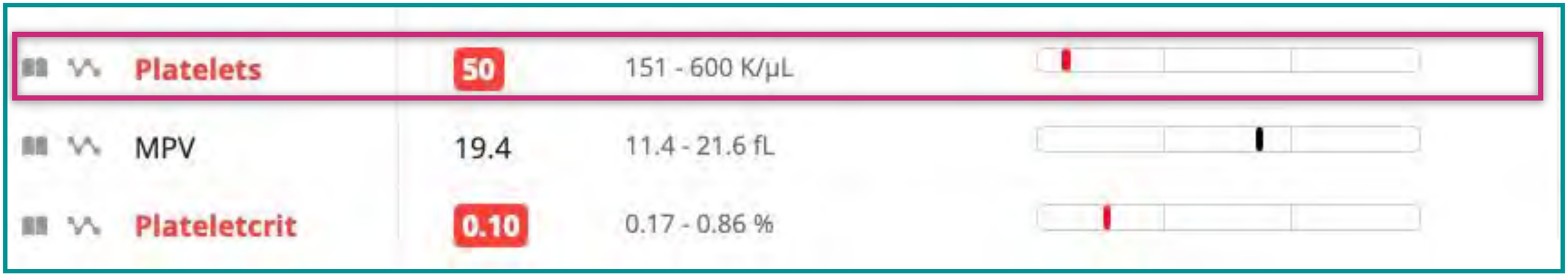
DDx For Monocytosis

- Chronic neutropenia
- Granulocyte colony-stimulating factor administration
- Increased endogenous or exogenous corticosteroids (especially in dogs)
- Inflammation (eg, infectious vs noninfectious, acute vs chronic)
- Monocytic or monoblastic leukemia (very rare)
- Necrosis and/or tissue destruction (eg, f… …mmune-mediated hemolytic anemia)
- Paraneopla… …ors (associated with poor prognosis)
  - …nocyte chemotactic protein; possible secretion of granulocyte-…ny-stimulating factor)
  - …steosarcoma

- Recovery from acute bone marrow injury
  - Secondary to administration of a chemotherapeutic agent
  - Secondary to parvovirus infection (rare)

But, are they really monocytes?

Simon-CBC-Platelets



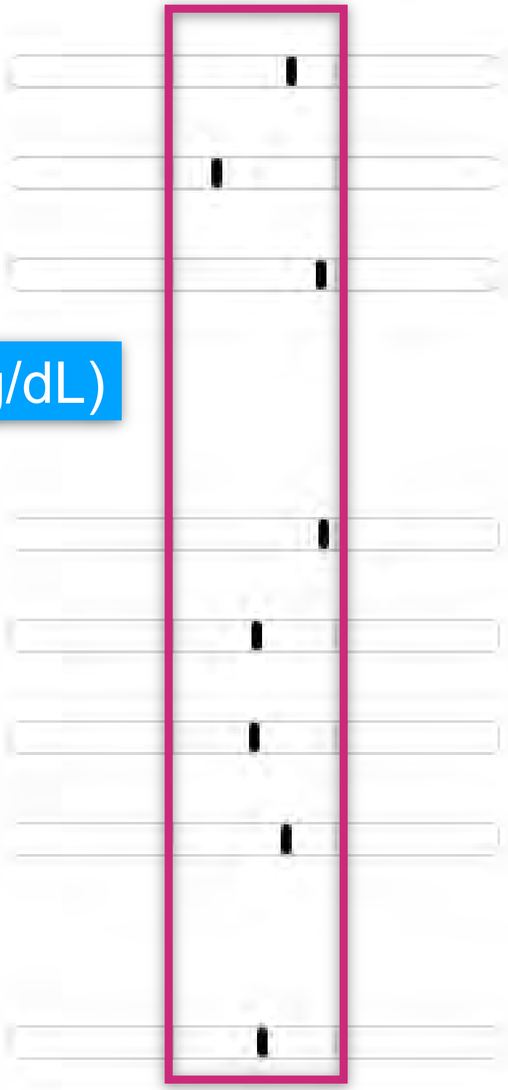
Platelets	50	151 - 600 K/µL
MPV	19.4	11.4 - 21.6 fL
Plateletcrit	0.10	0.17 - 0.86 %

Always evaluate blood smear and/or dot plots for platelet clumping!

Simon-CBC-Chemistry 1

Glucose	139	71 - 159 mg/dL
Creatinine	1.2	0.8 - 2.4 mg/dL
Urea	35	16 - 36 mg/dL
BUN: Creatinine Ratio	30	
Phosphorus	7.4	3.1 - 7.5 mg/dL
Calcium	9.7	7.8 - 11.3 mg/dL
Sodium	158	150 - 165 mmol/L
Potassium	5.2	3.5 - 5.8 mmol/L
Na: K Ratio	30	
Chloride	122	112 - 129 mmol/L

SDMA 40 µg/dL (0-14 µg/dL)



Simon-UA

Collection	Cystocentesis	
Colour	Dark Yellow	
Clarity	Clear	
Specific Gravity	1.024	
pH	6.0	
Urine Protein	TR	
Glucose	neg	
Ketones	neg	
Blood / Haemoglobin	250	Ery/µL
Bilirubin	3	mg/dL
Urobilinogen	8	mg/dL

White Blood Cells	1 /HPF
Red Blood Cells	6 /HPF
Bacteria, Cocci	Suspect presence
Bacteria, Rods	None detected
Squamous Epithelial Cells	None detected
Non-Squamous Epithelial Cells	<1 /HPF
Hyaline Casts	None detected
Non-Hyaline Casts	None detected
Calcium Oxalate Dihydrate Crystals	None detected
Struvite Crystals	None detected
Ammonium Biurate Crystals	None detected
Bilirubin Crystals	None detected
Unclassified Crystals	<1 /HPF

Are There Non-Renal Causes Of High SDMA?

- Yep…
- Greyhounds (RI: 0-20µg/dL)
  - https://www.idexx.com/files/diagnostic-update-greyhound-specific-reference-intervals.pdf
- Lymphoma and lymphoid leukemias

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DOI: 10.1111/vco.12845

Veterinary and Comparative Oncology

WILEY

ORIGINAL ARTICLE

The association between symmetric dimethylarginine concentrations and various neoplasms in dogs and cats

Michael J. Coyne | Corie Drake | Donald J. McCrann | David Kincaid

1803 dogs and cats with neoplasia

TABLE 1 Median SDMA and Cr concentrations by tumour type

Tumour type	SDMA µmol/L (range)			Cr µmol/L (range)		
	Case animals	Control animals	*p* value	Case animals	Control animals	*p* value
Canine hemangiosarcoma	0.54 (0.1–1.53)	0.49 (0.2–2.97)	.136	79.6 (17.7–265.2)	79.6 (26.5–875.2)	.105
Canine lipoma	0.44 (0.1–1.24)	0.49 (0.15–2.03)	.004	79.6 (26.5–229.8)	79.6 (26.5–415.5)	.099
Canine lymphoma	3-98.8 µg/dL	0.49 (0.15–2.47)	<.0001	79.6 (17.7–406.6)	79.6 (35.4–919.4)	.897
Canine mammary adenocarcinoma	0.44 (0.1–1.33)	0.49 (0.1–2.82)	.006	61.9 (26.5–327.1)	70.7 (26.5–724.9)	<.0001
Canine mammary carcinoma	0.44 (0.1–2.22)	0.49 (0.05–4.94)	.008	61.9 (26.5–229.8)	79.6 (17.7–574.6)	<.0001
Feline lymphoma	2-98.8 µg/dL	0.54 (0.15–3.46)	<.0001	114.9 (44.2–1007.8)	123.8 (53.0–795.6)	<.0001
Feline visceral mast cell tumour	0.64 (0.25–1.93)	0.54 (0.25–4.35)	.566	132.6 (53.0–716.1)	132.6 (44.2–539.3)	.826

Cancer type	*N*	OR (95% CI)	*p*
Canine lymphoma	307	10.00 (5.98–16.72)	$p < .001$
Feline lymphoma	224	3.04 (1.95–4.73)	$p < .001$
Feline visceral mast cell tumour	55	1.63 (0.67–3.92)	$p = .275$
Canine hemangiosarcoma	230	1.11 (0.66–1.87)	$p = .691$
Canine mammary carcinoma	387	0.49 (0.28–0.84)	$p = .009$
Canine mammary adenocarcinoma	388	0.41 (0.231–0.71)	$p = .001$
Canine lipoma	212	0.39 (0.18–0.85)	$p = .013$

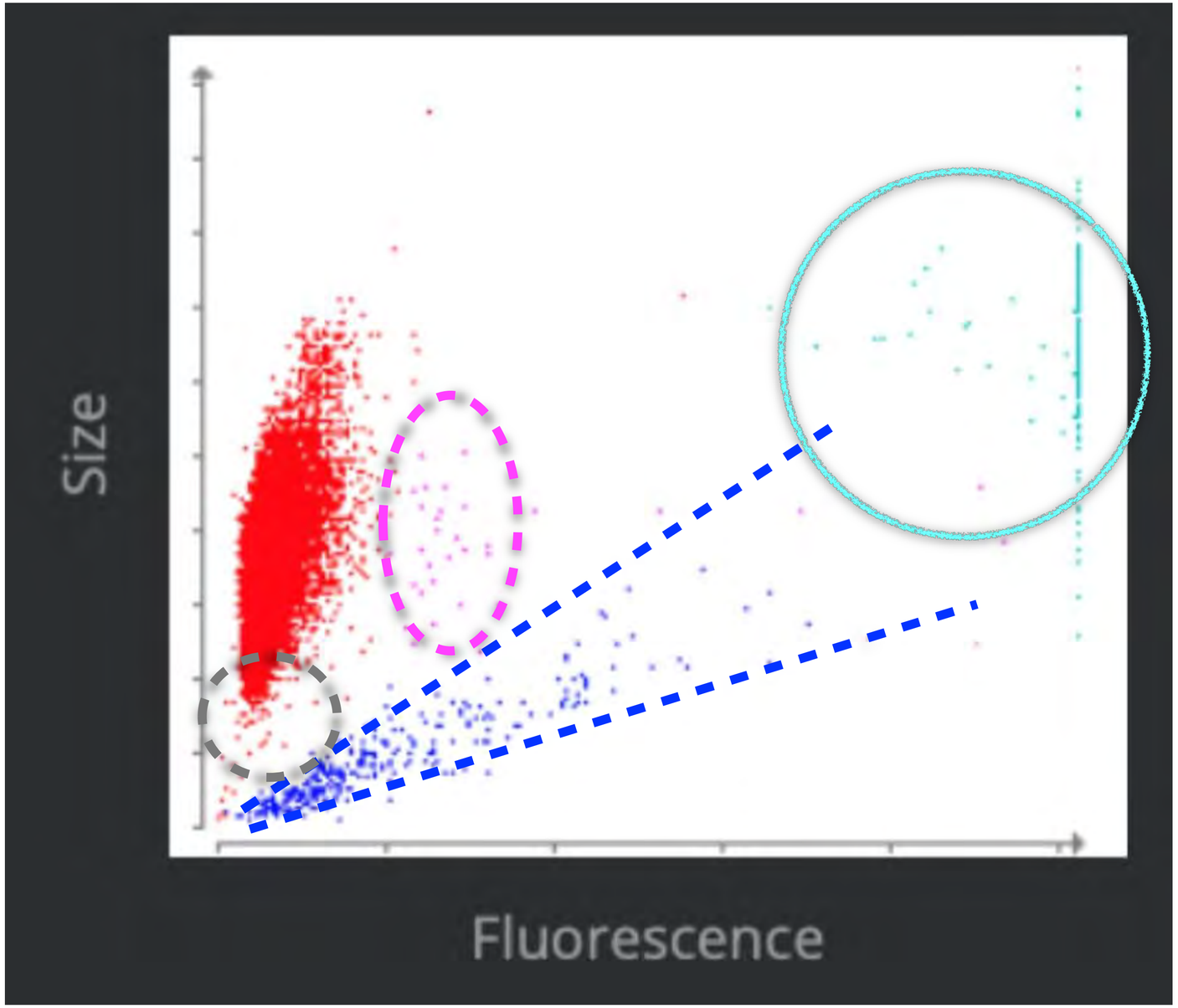
RESEARCH ARTICLE PLOS ONE | https://doi.org/10.1371/journal.pone.0250839 May 14, 2021

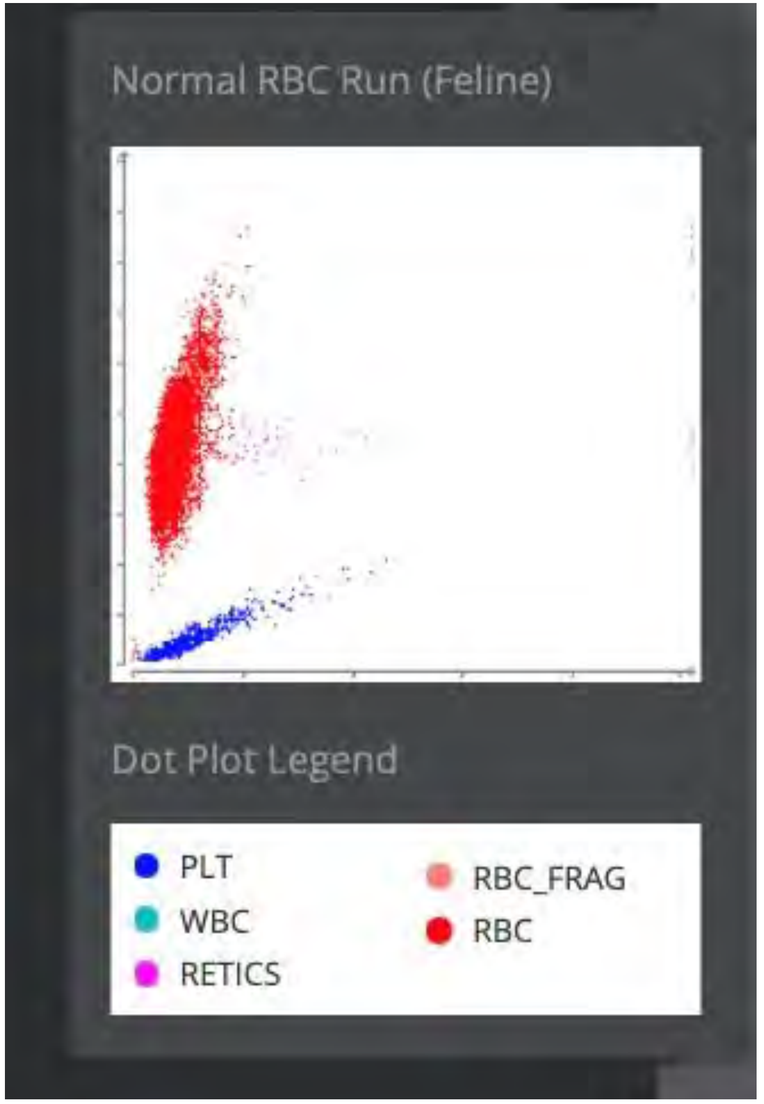
Validation of protein arginine methyltransferase 5 (PRMT5) as a candidate therapeutic target in the spontaneous canine model of non-Hodgkin lymphoma

Shelby L. Sloan[1,2☯], Kyle A. Renaldo[3☯], Mackenzie Long[1,2], Ji-Hyun Chung[2], Lindsay E. Courtney[3], Konstantin Shilo[4], Youssef Youssef[2], Sarah Schlotter[2], Fiona Brown[2], Brett G. Klamer[5], Xiaoli Zhang[5], Ayse S. Yilmaz[5], Hatice G. Ozer[5], Victor E. Valli[6†], Kris Vaddi[7], Peggy Scherle[7], Lapo Alinari[2], William C. Kisseberth[2,3‡*], Robert A. Baiocchi[2‡*]

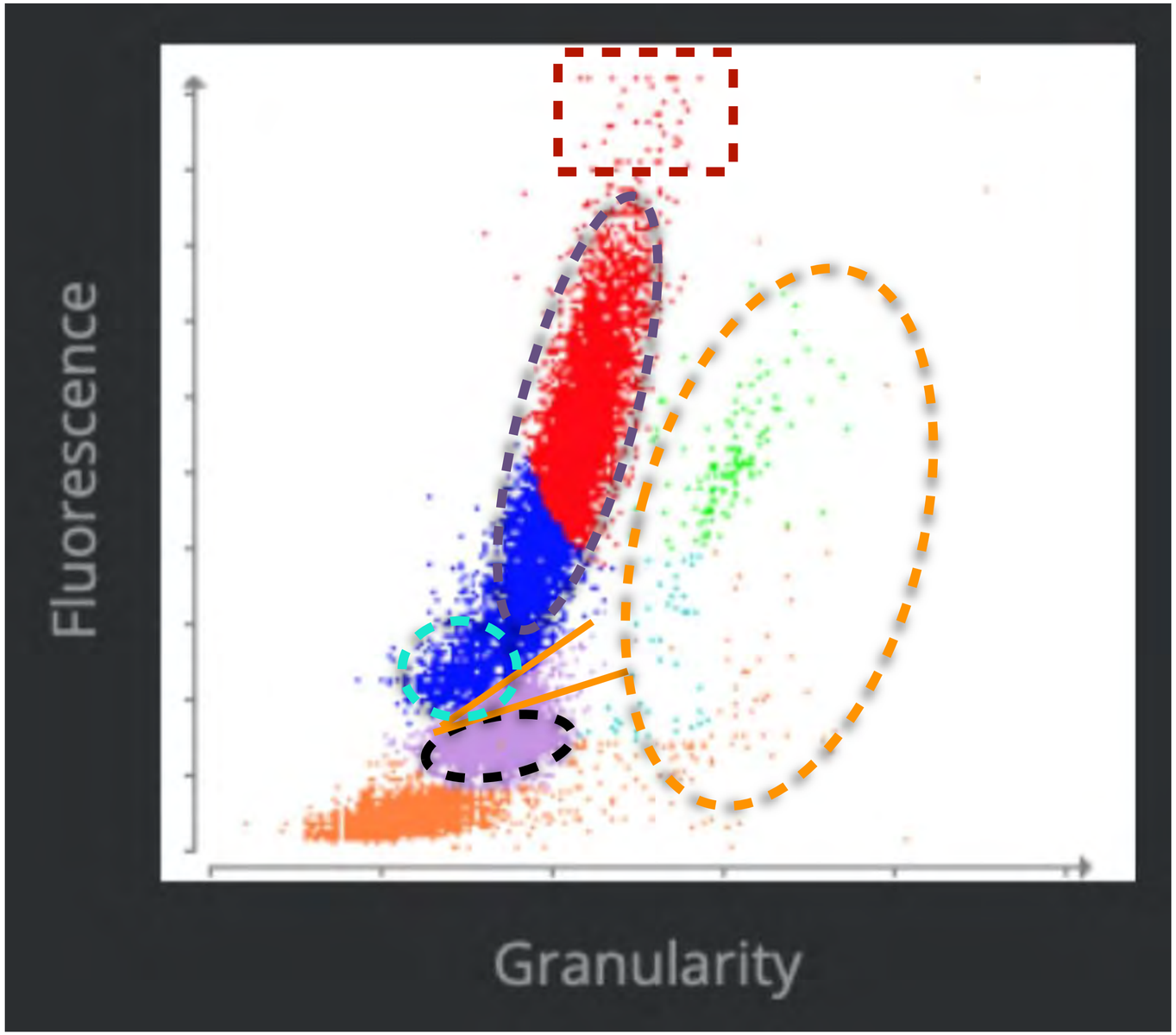
- 42.4% of lymphomas positive for PRMT5
- PRMT5 inhibition → Cell death

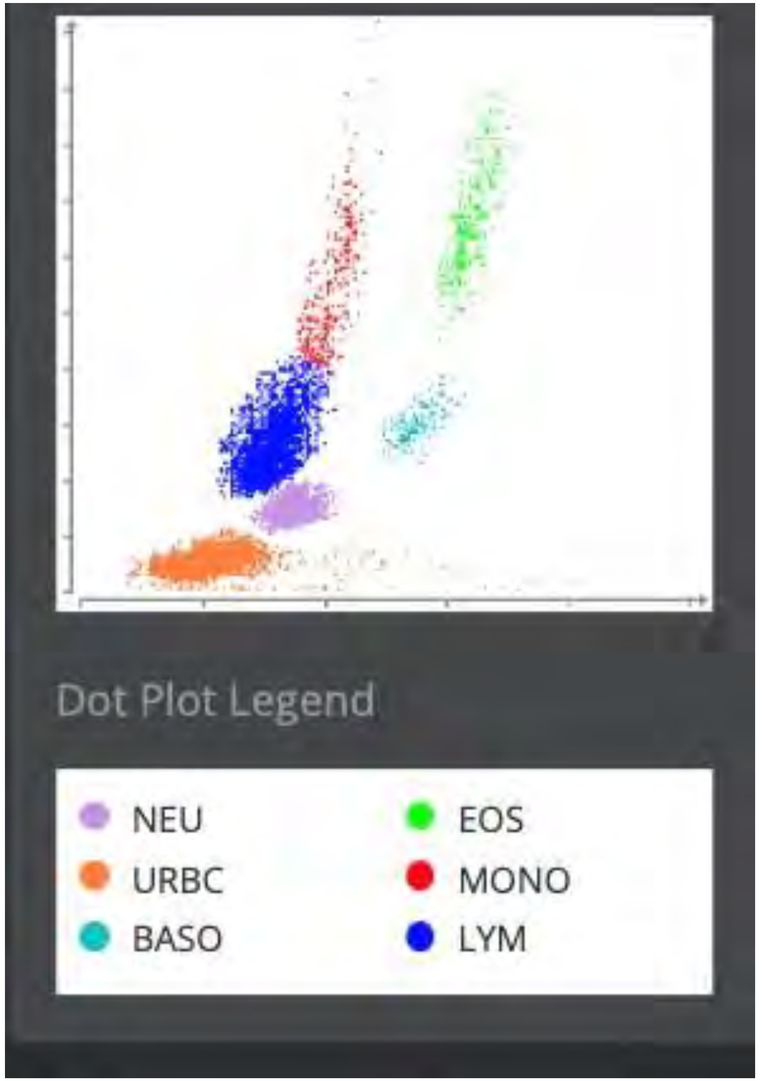
Simon-RBC Dot Plots

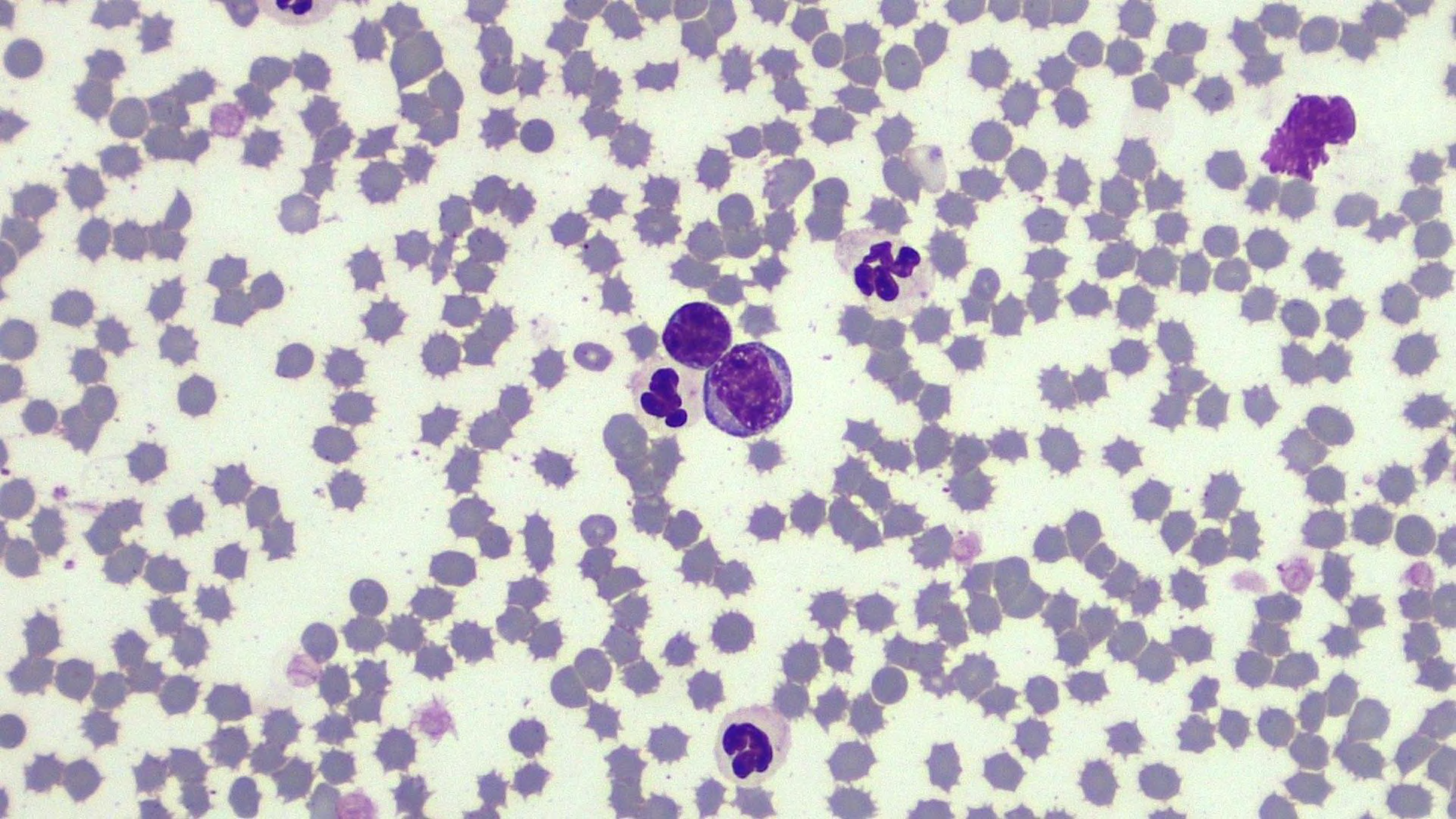


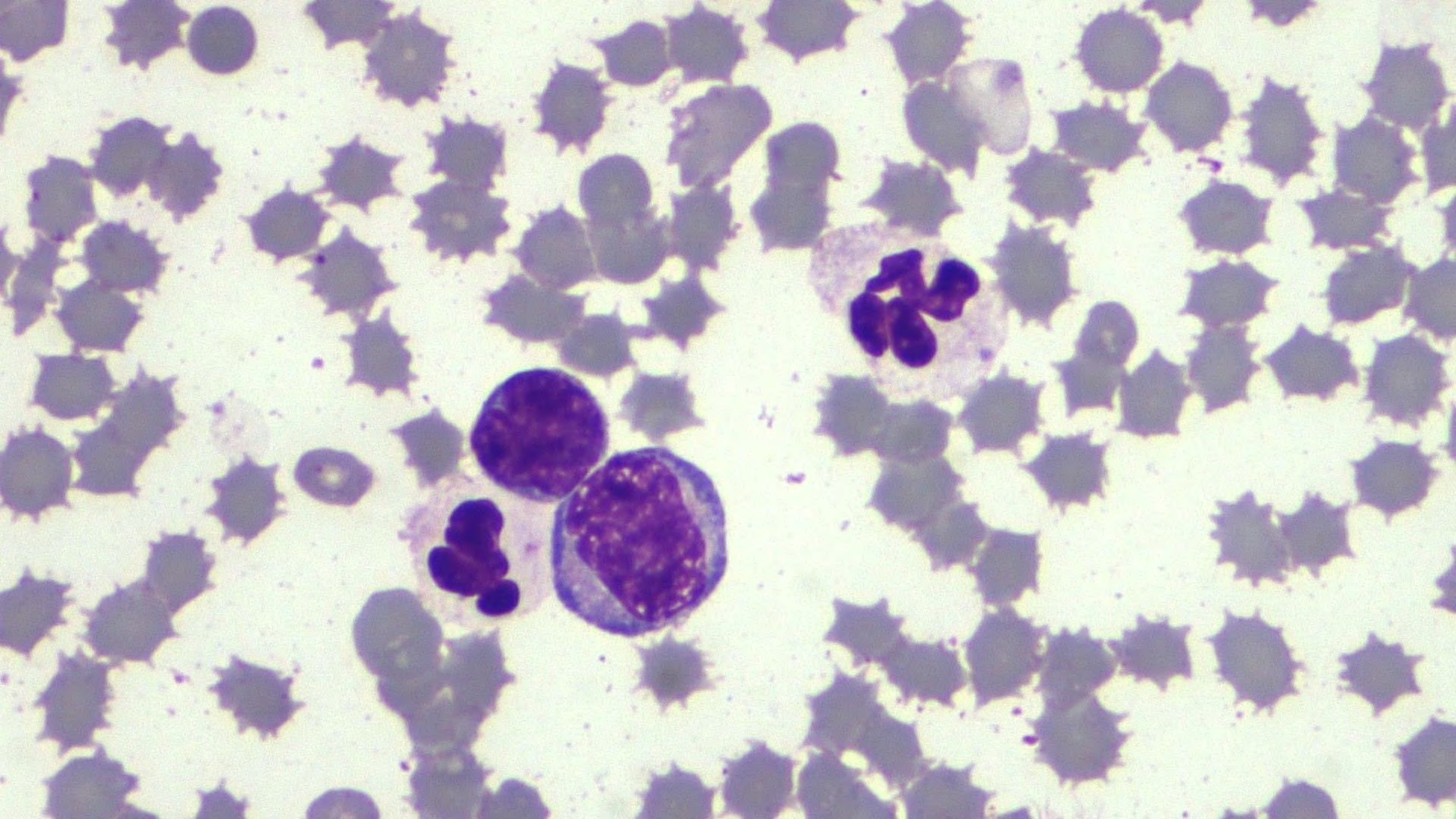


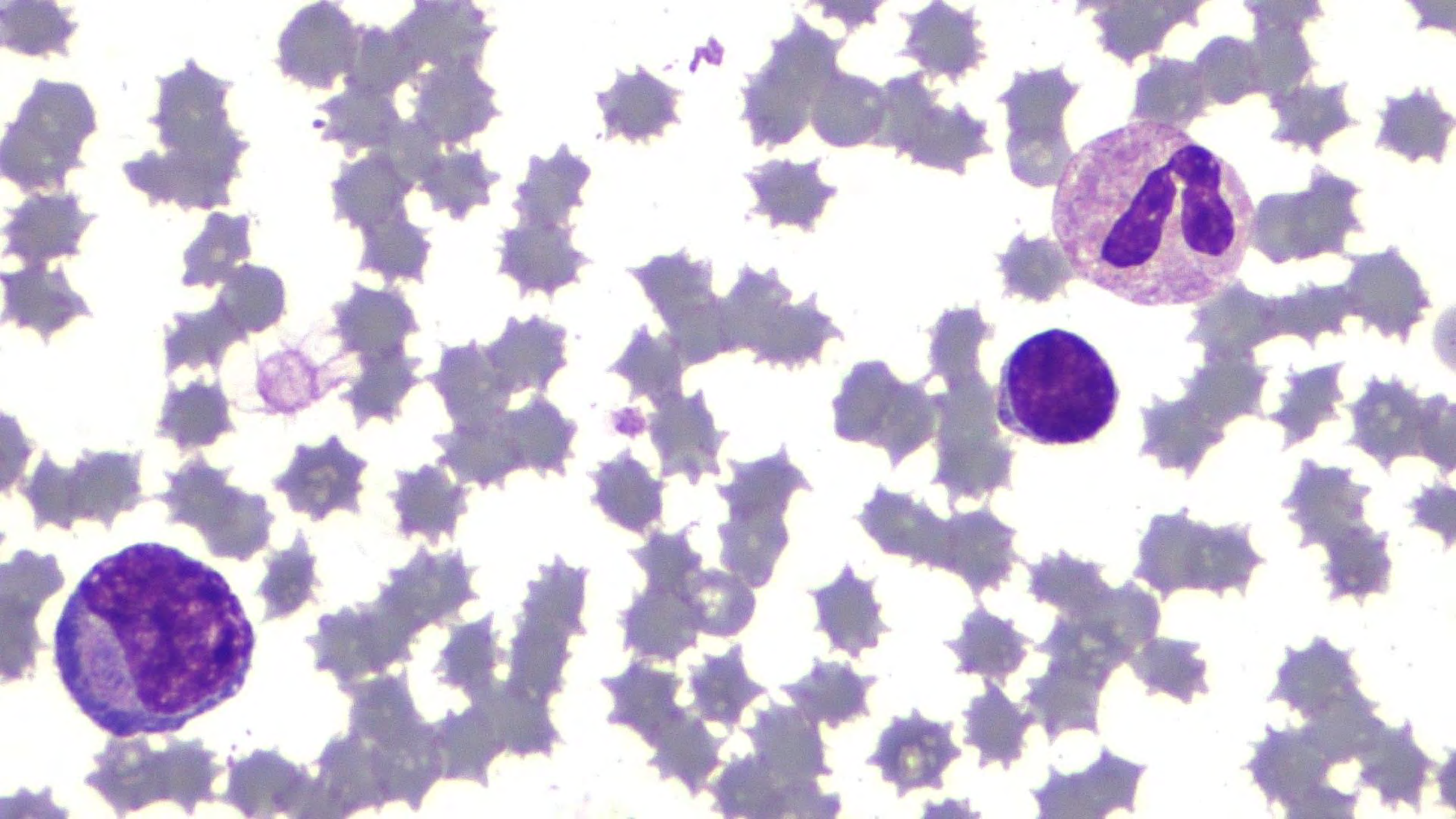
Simon-WBC Dot Plots

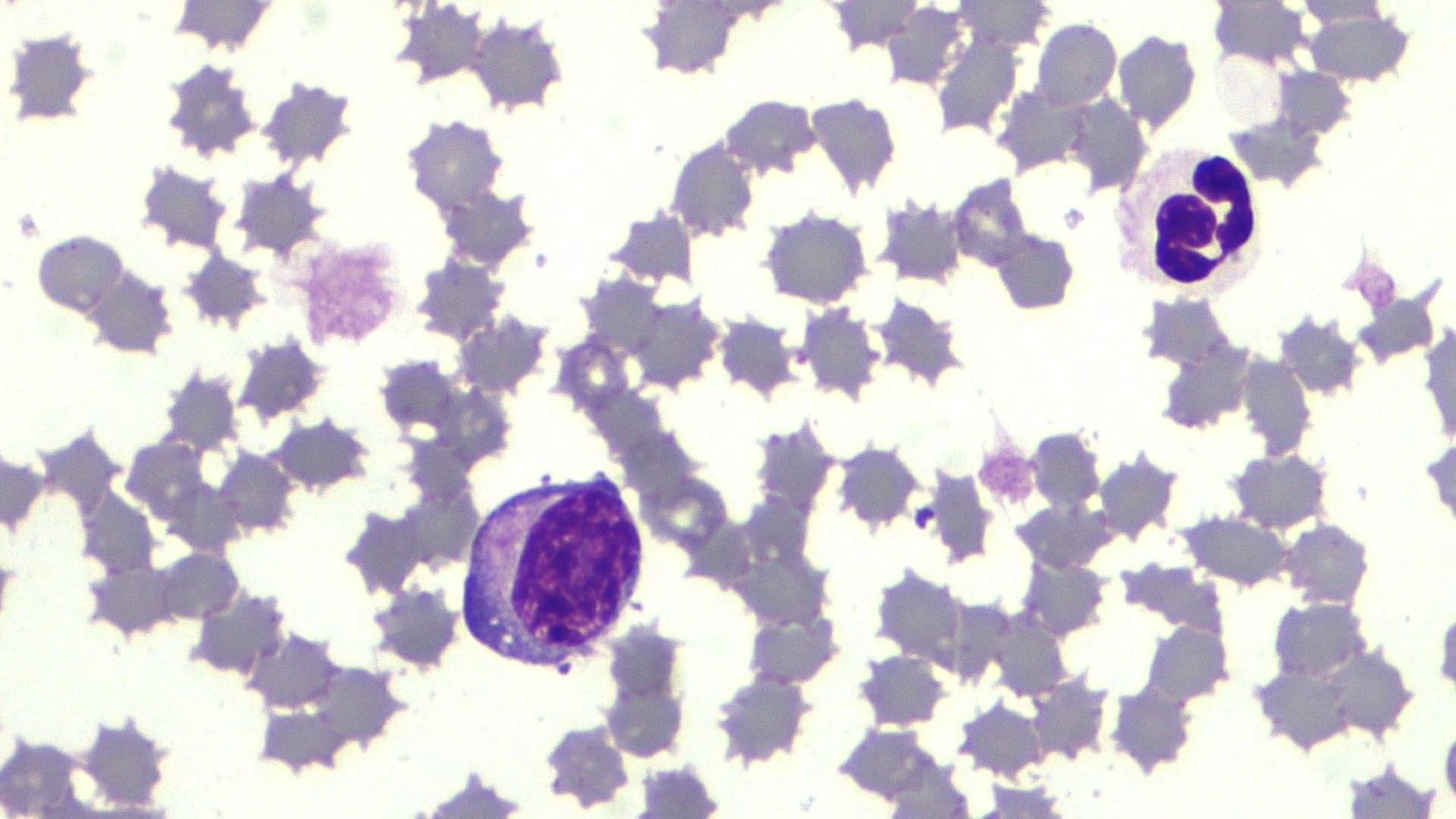




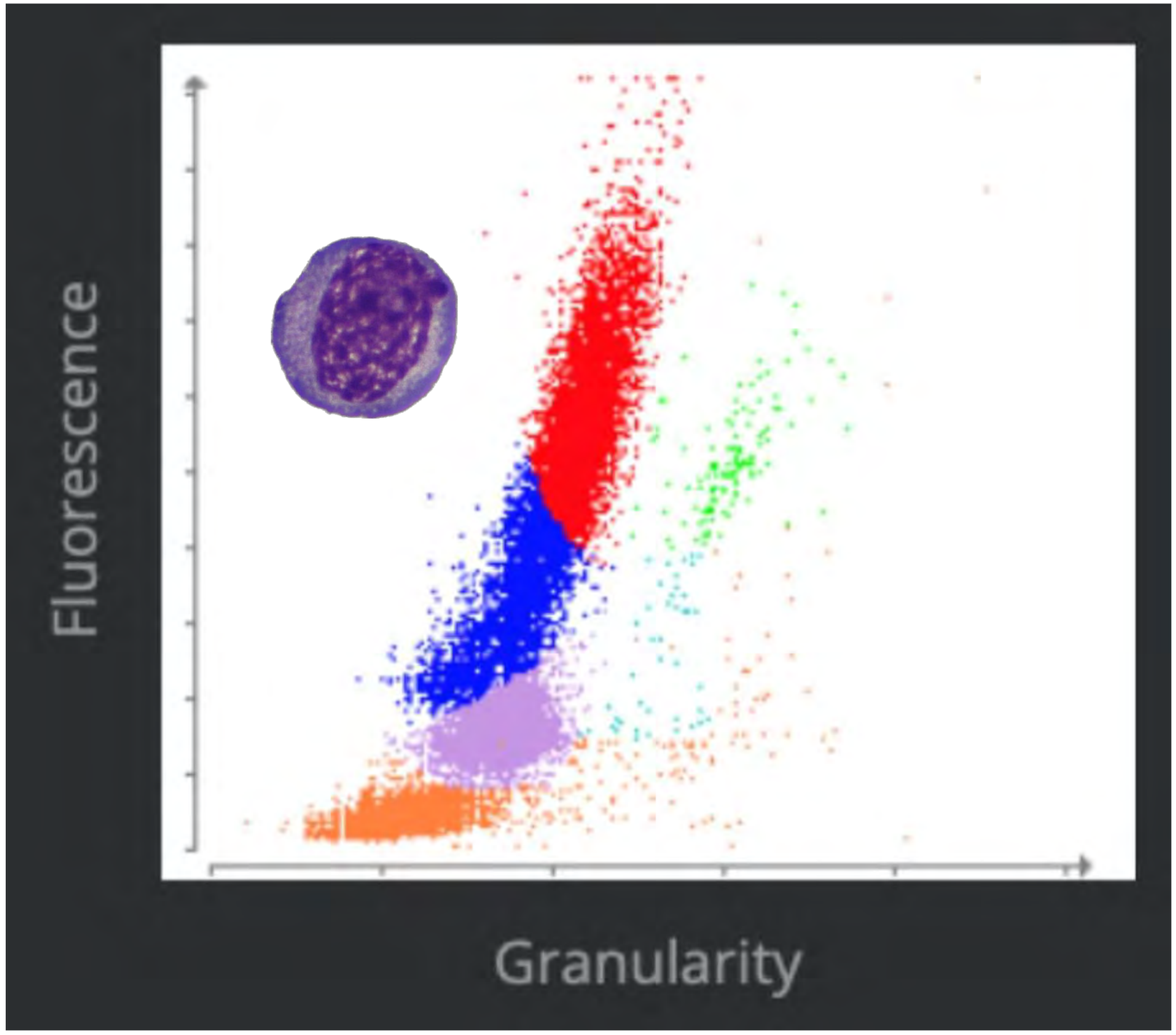


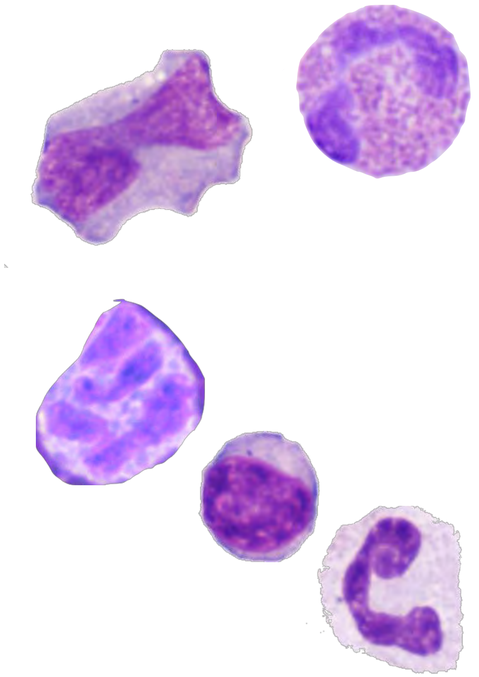






Simon-WBC Dot Plots





“Simon”

- Owners elected not to treat him