

Myelodysplastic Syndromes: Disease, Diagnosis, & Treatment

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Myelodysplastic Syndrome

Myelo = bone marrow cells

dysplastic = funny looking

Syndrome = group of symptoms

1

Picasso 1 Premise

Picasso



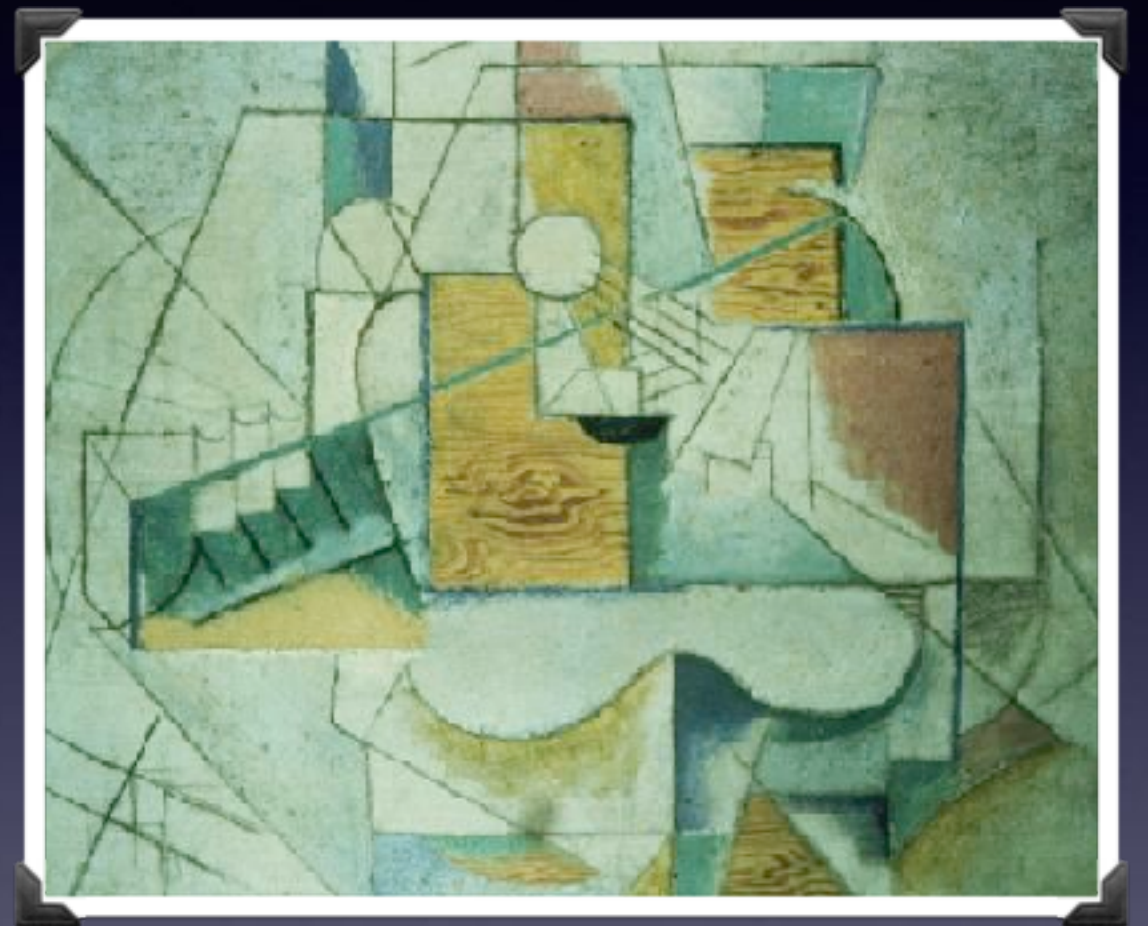
Guitar on a Table

Cogle



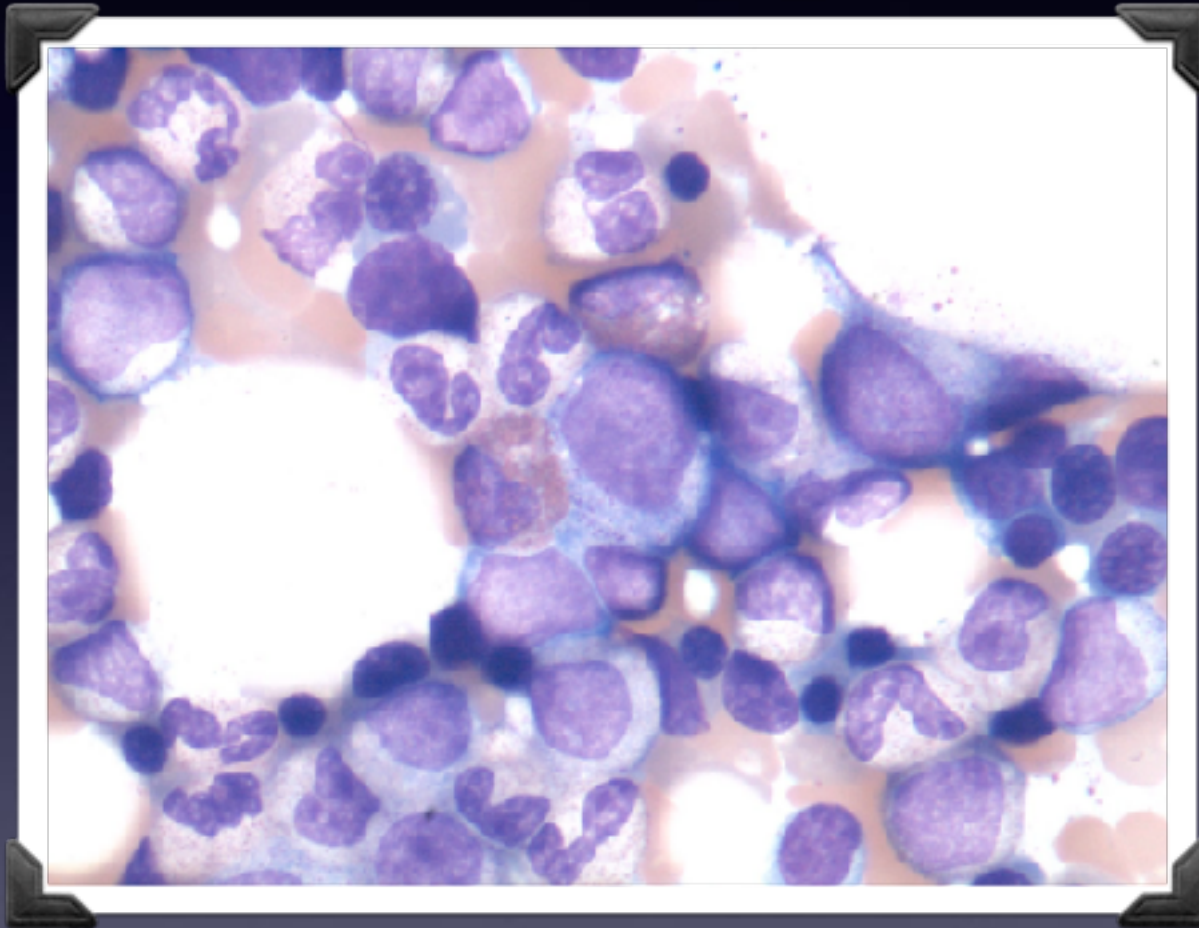
Guitar on a Table

Picasso

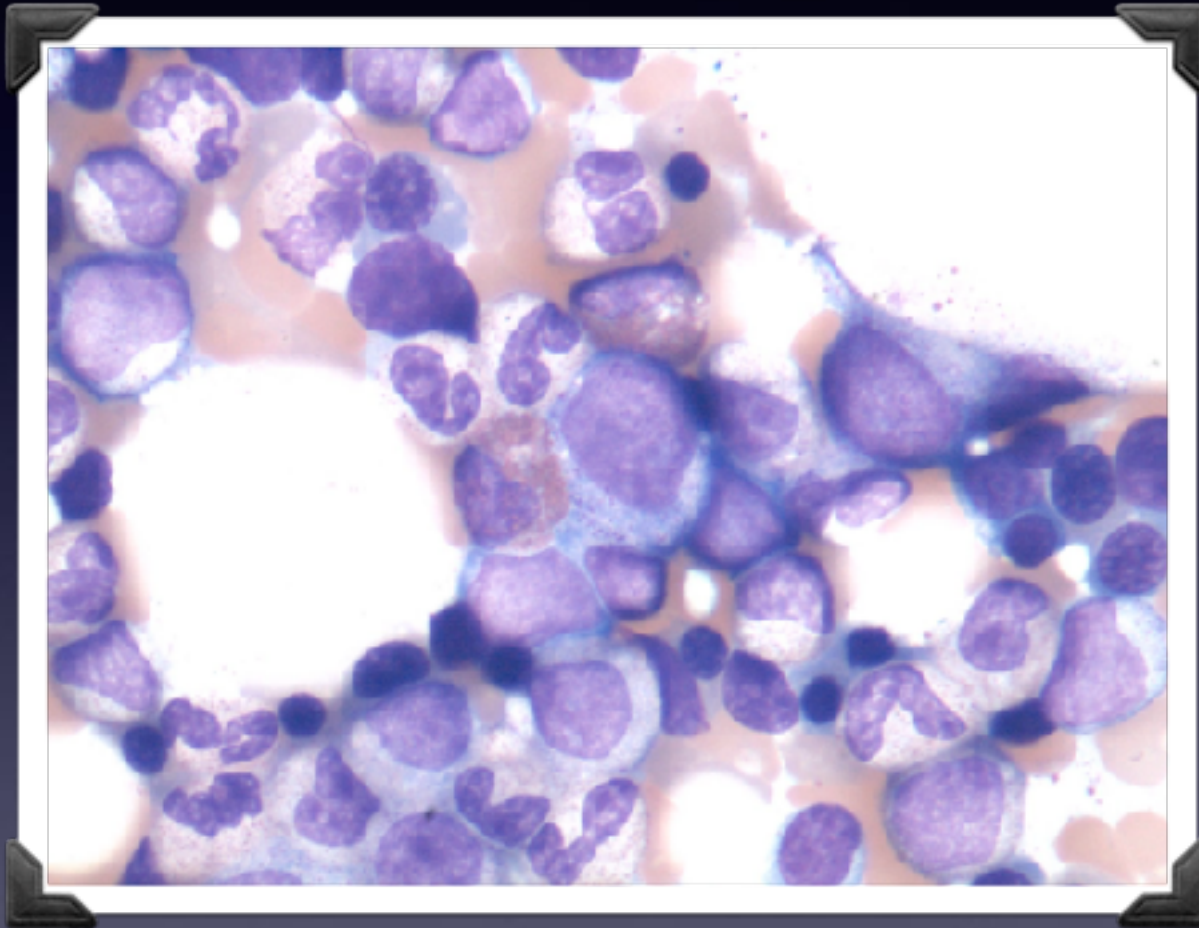


Guitar on a Table

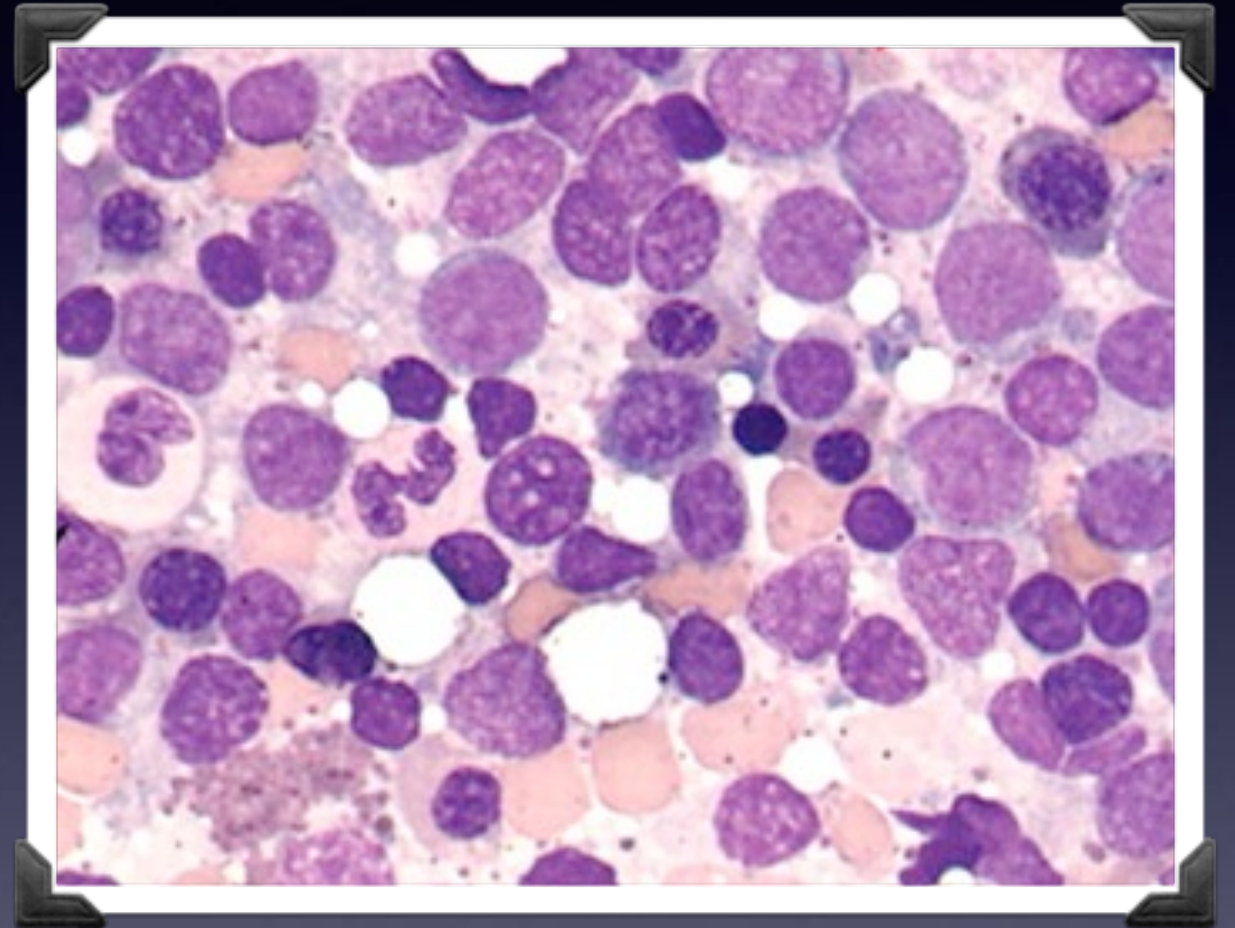
Normal Bone Marrow



Normal Bone Marrow



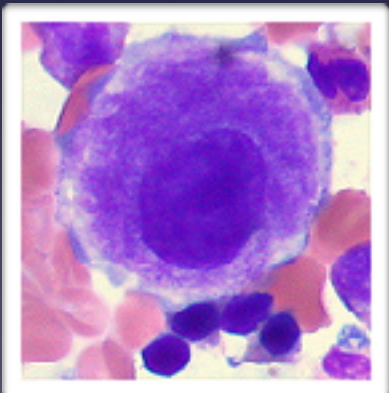
MDS



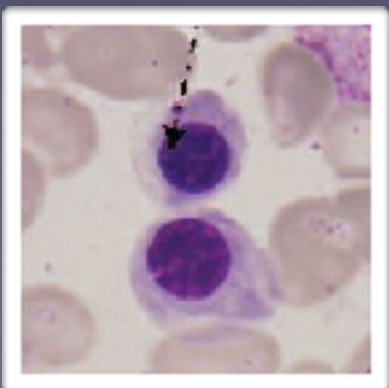
4 pathologists walk into a room ...



myeloid

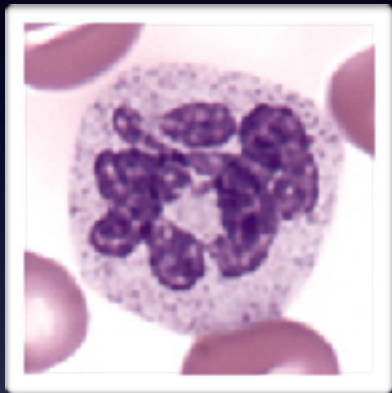


megakaryocyte



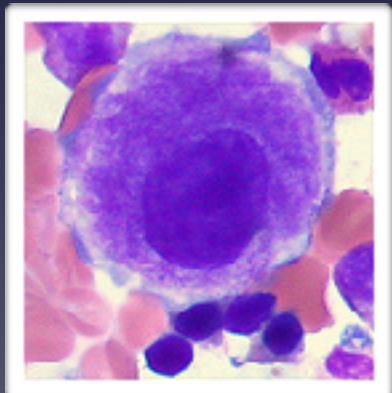
erythroid

4 pathologists walk into a room ...



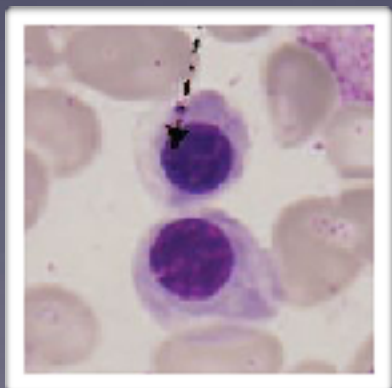
myeloid

89% agreement



megakaryocyte

91% agreement

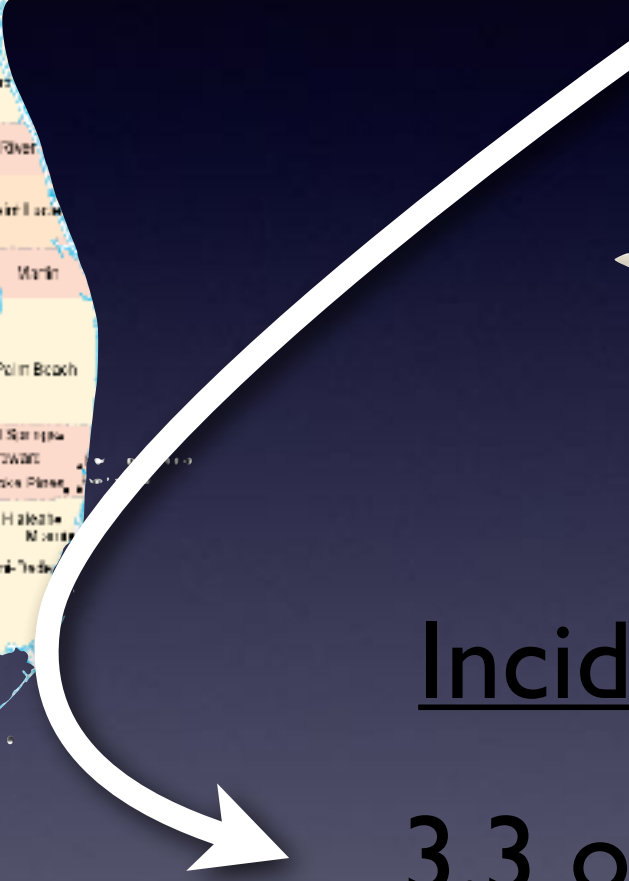


erythroid

75% agreement

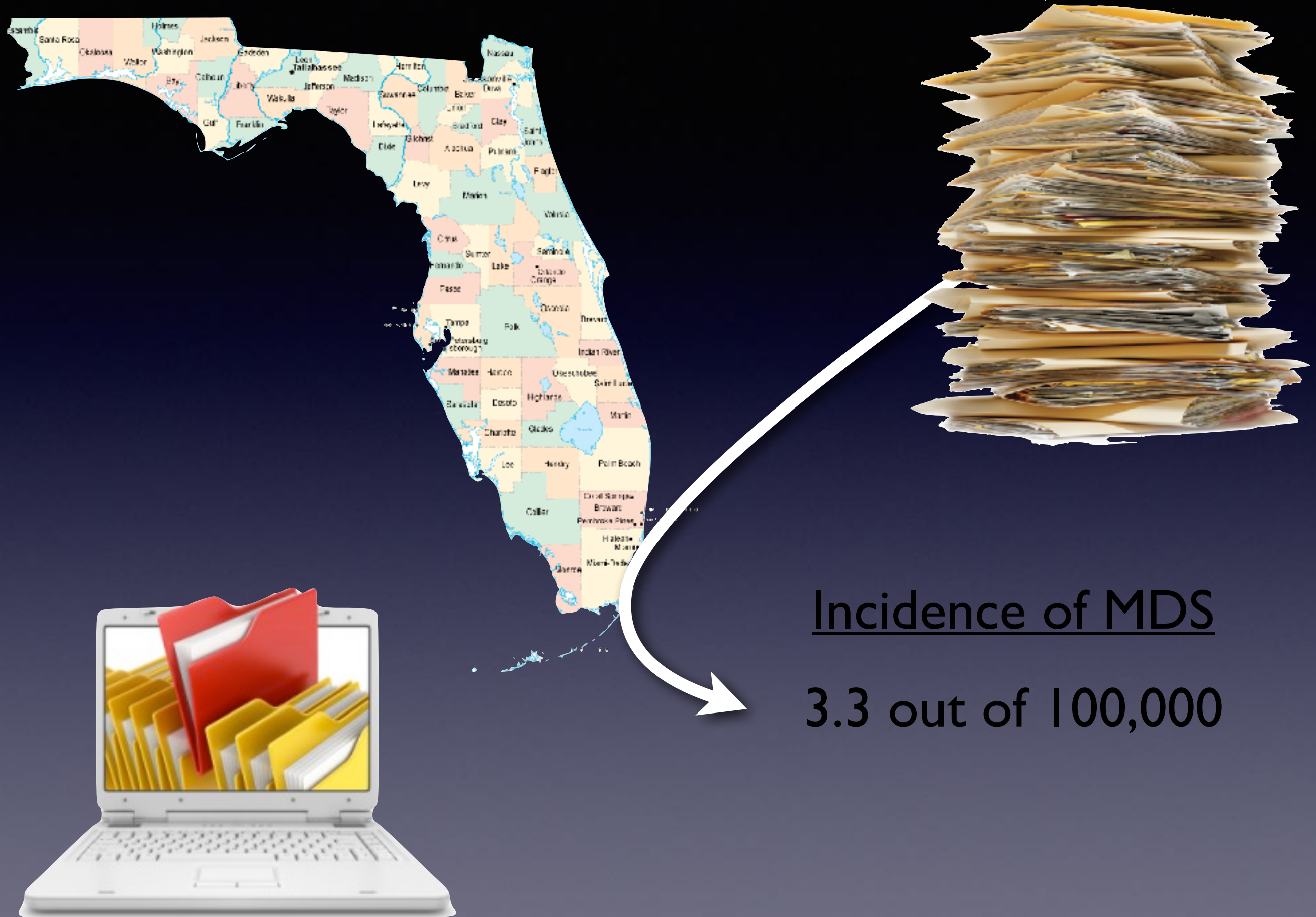


Incidence of MDS



Incidence of MDS

3.3 out of 100,000



Incidence of MDS

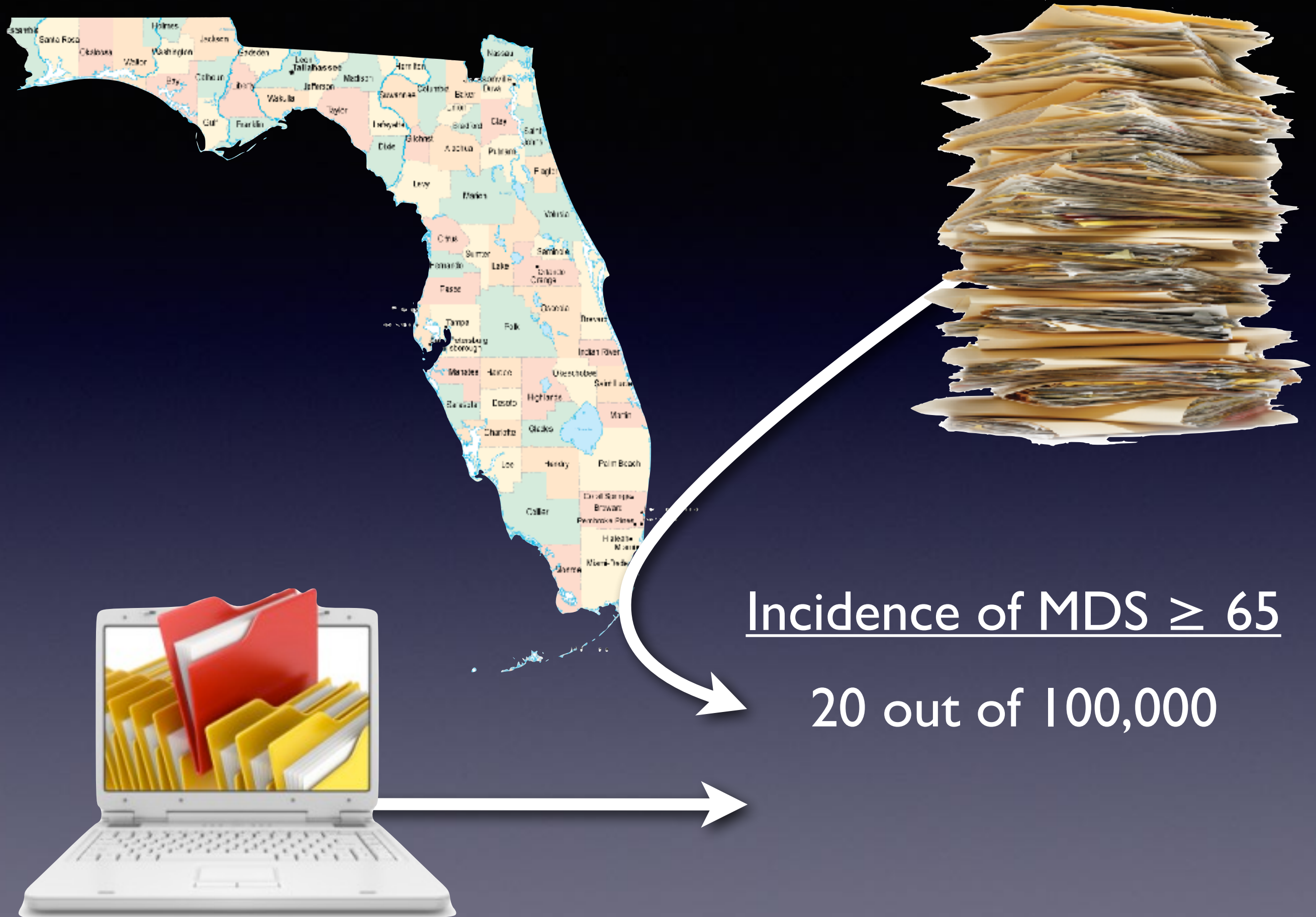
3.3 out of 100,000



Incidence of MDS

~~3.3 out of 100,000~~

5.3 out of 100,000





Incidence of MDS \geq 65

~~20 out of 100,000~~

75 out of 100,000

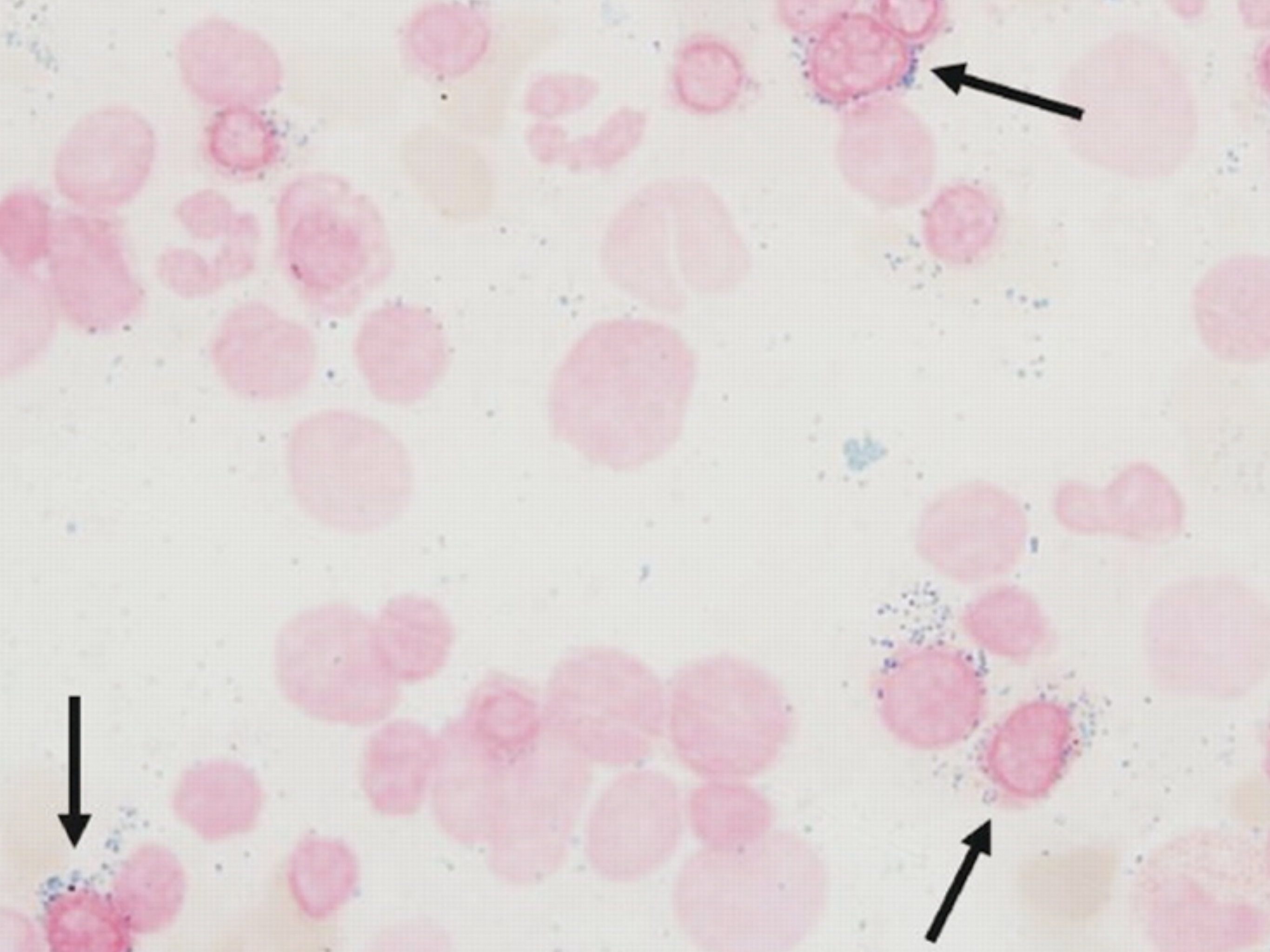
MDS

10,000 people diagnosed each year in US

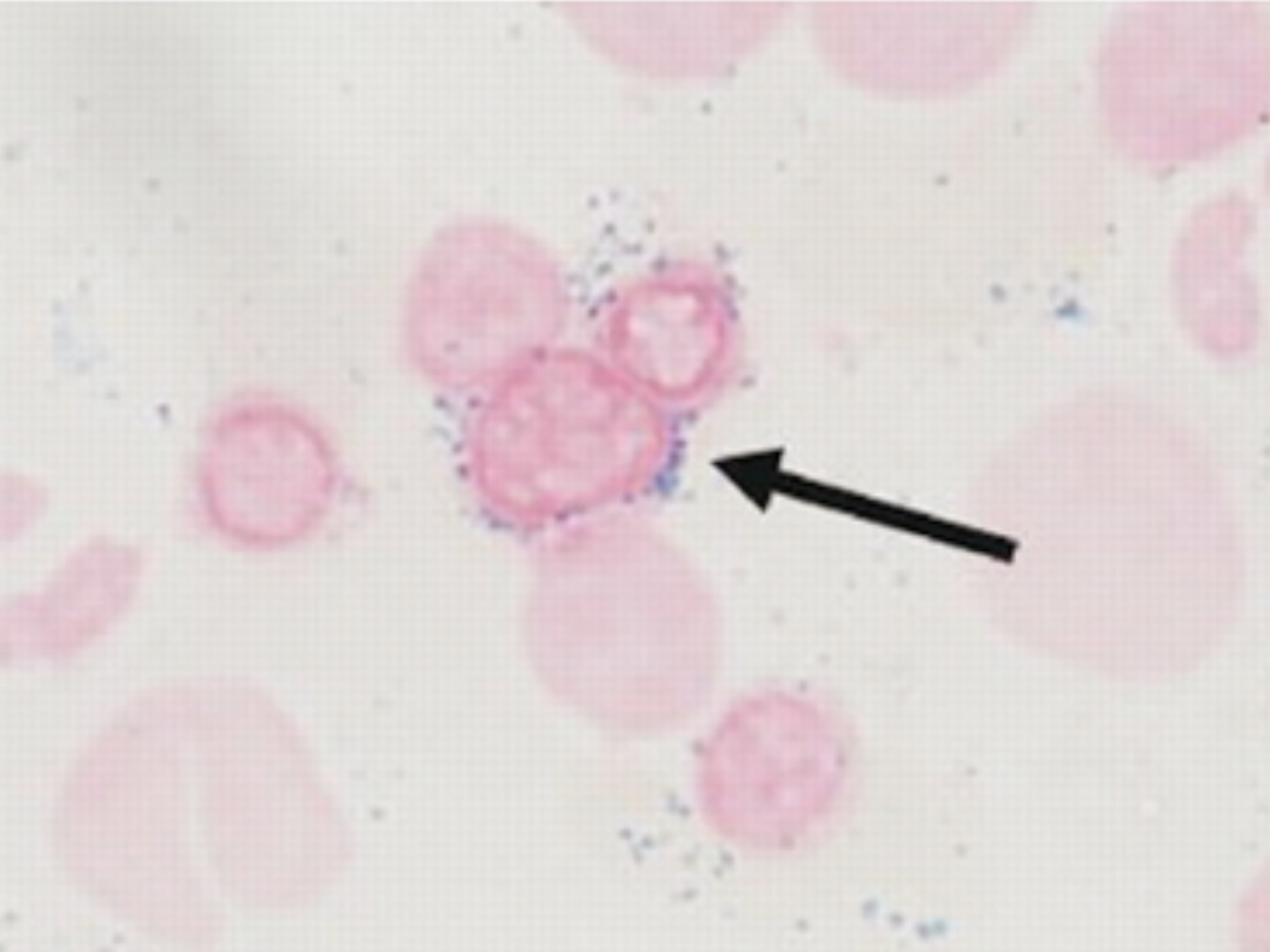
60,000 - 170,000 MDS currently in US

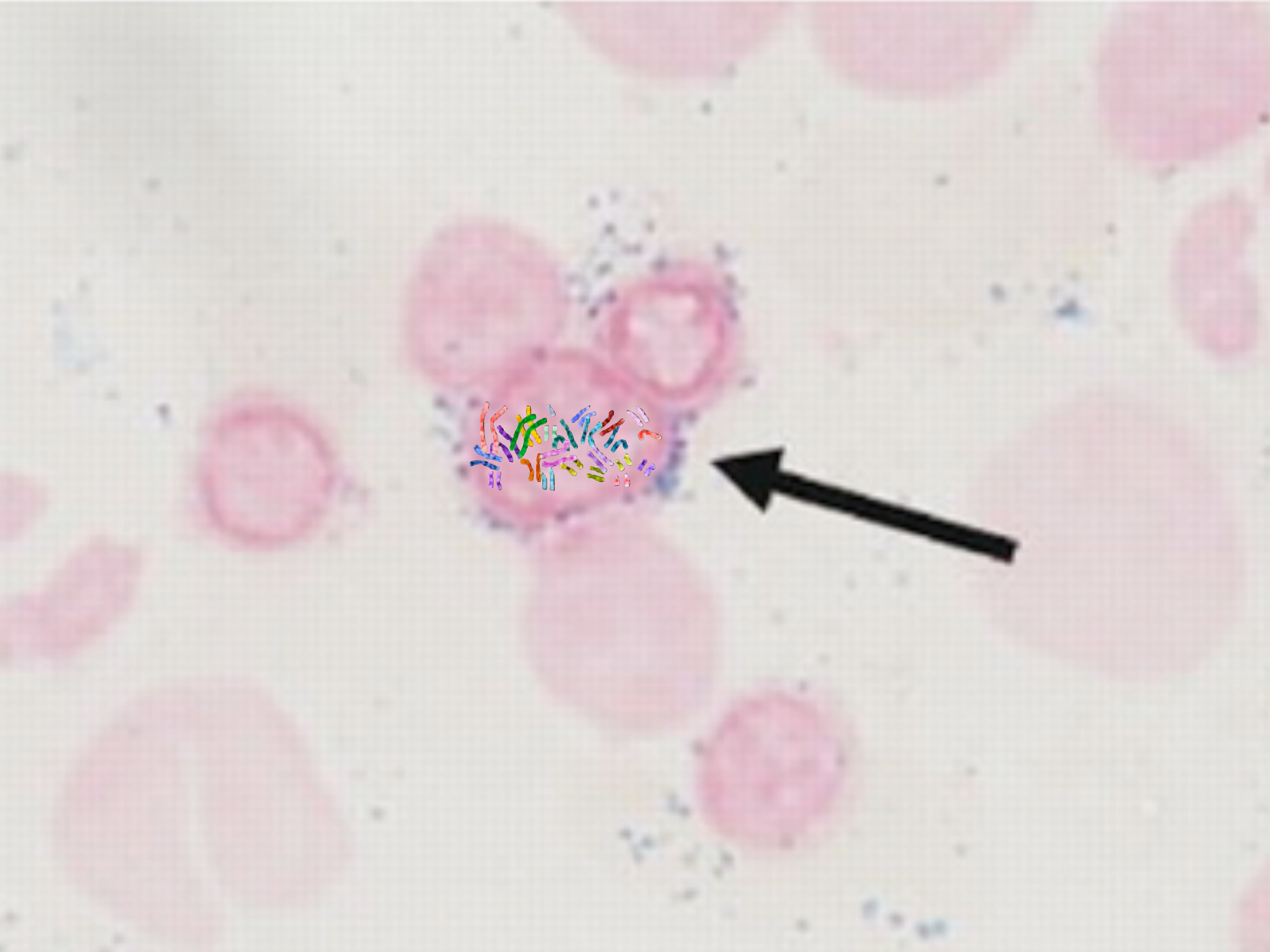
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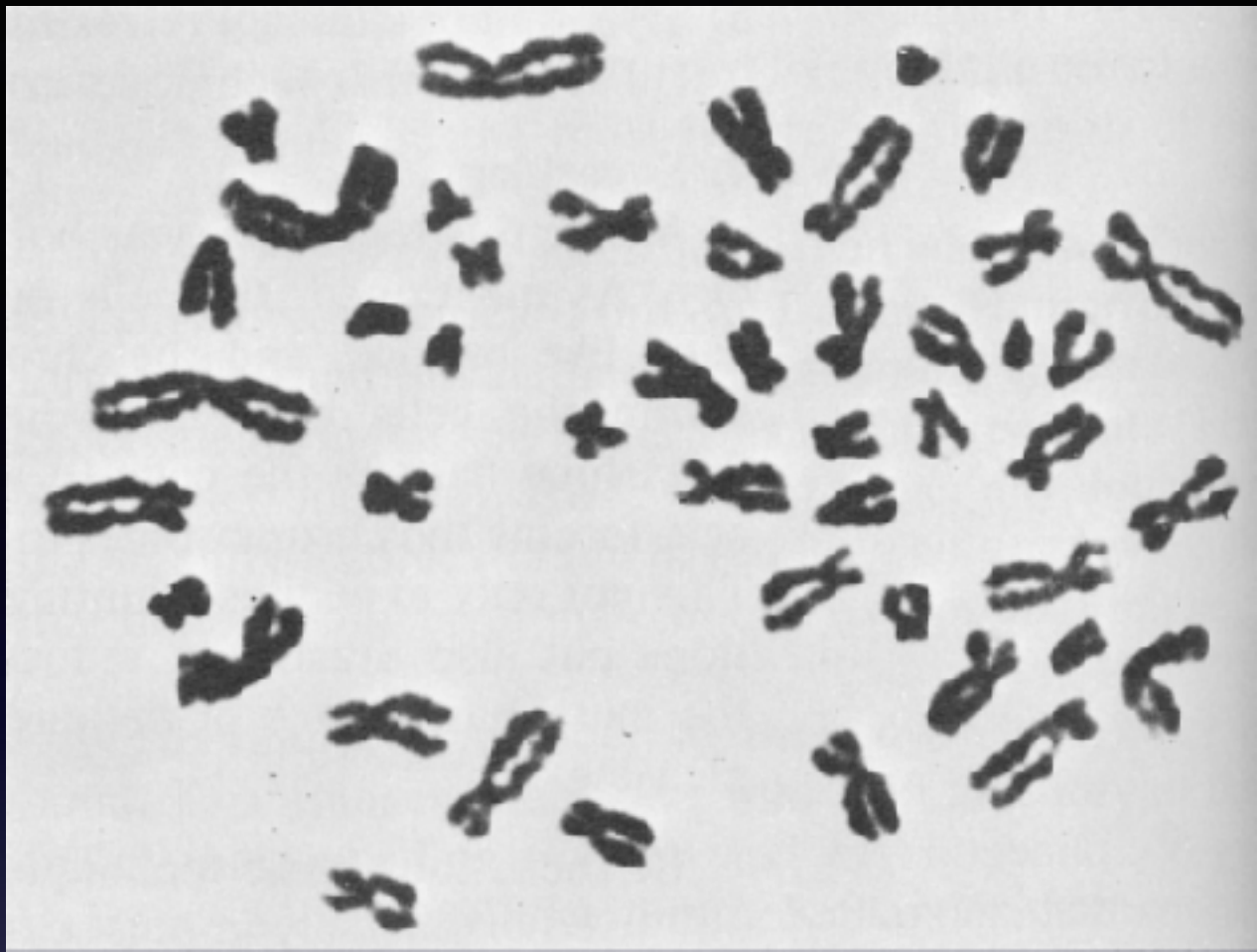
Software Bugs

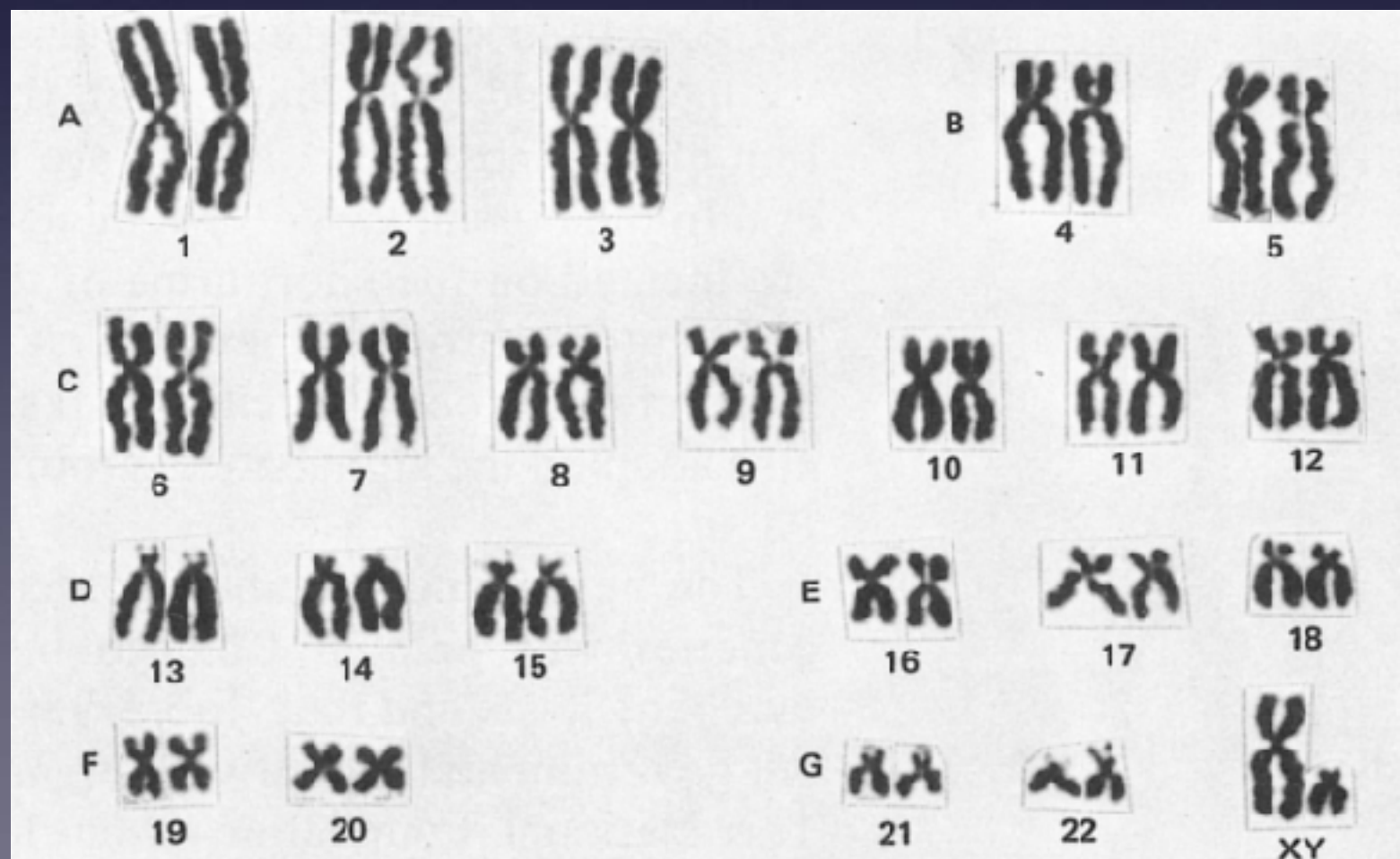
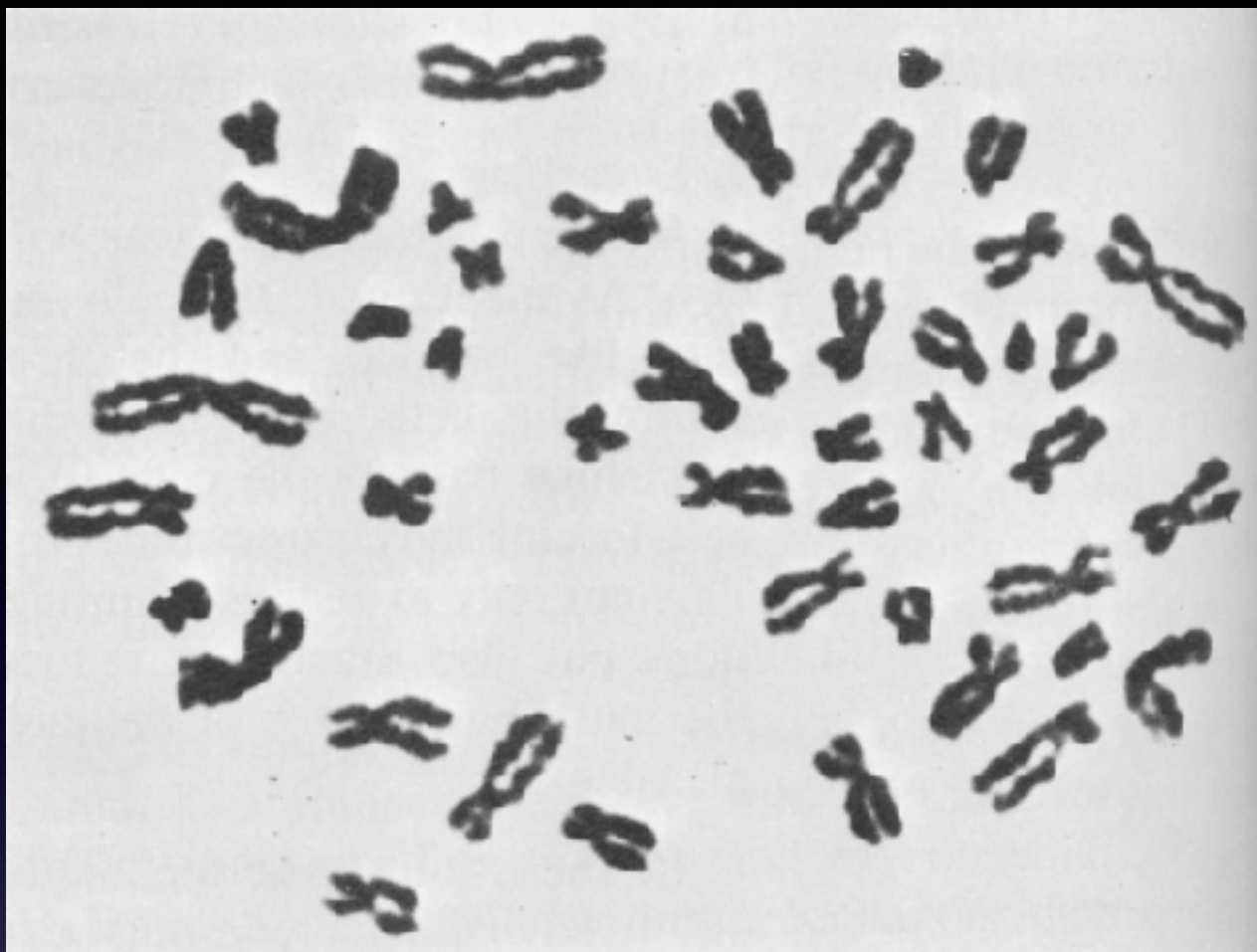












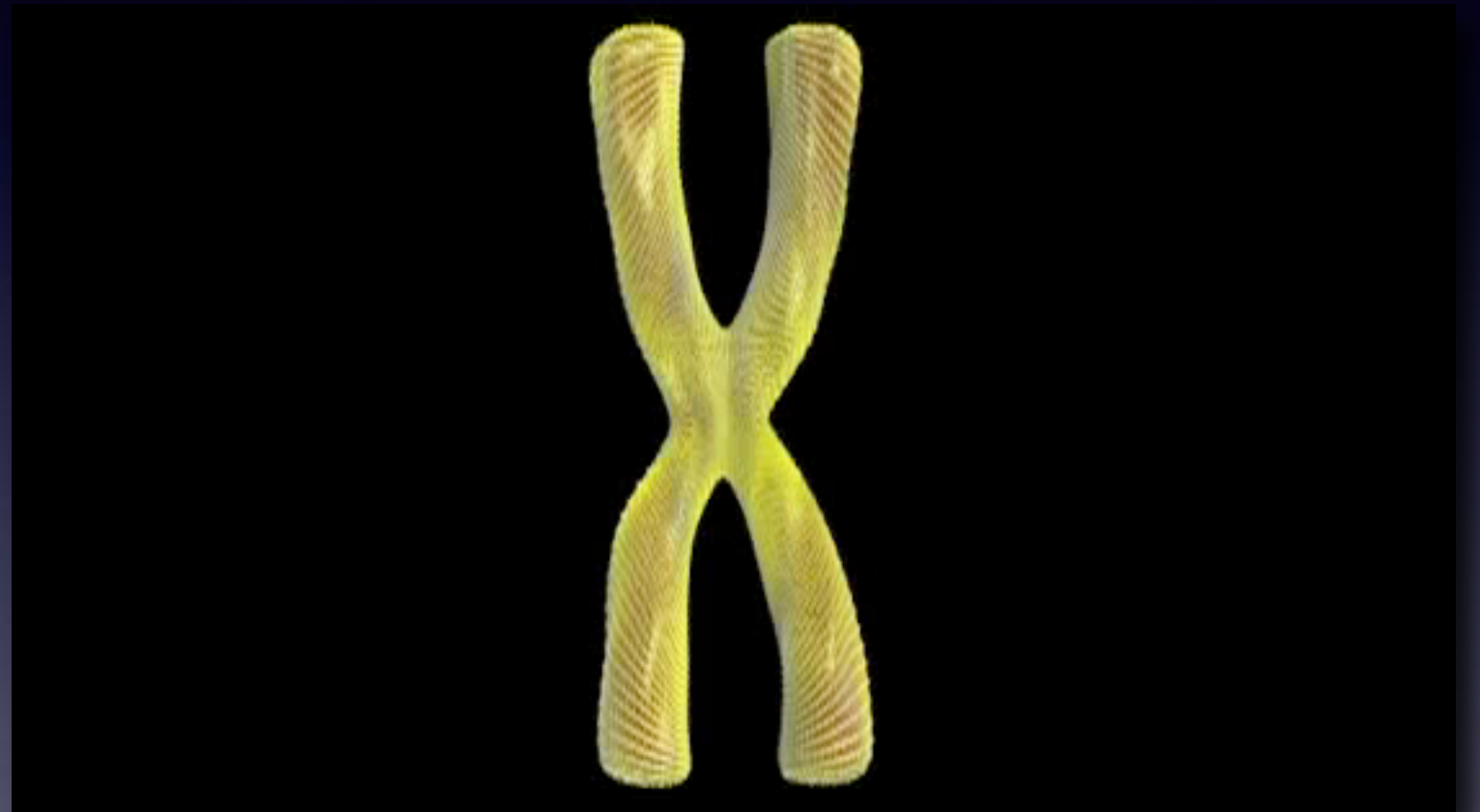
Chromosomes



Genes



DNA



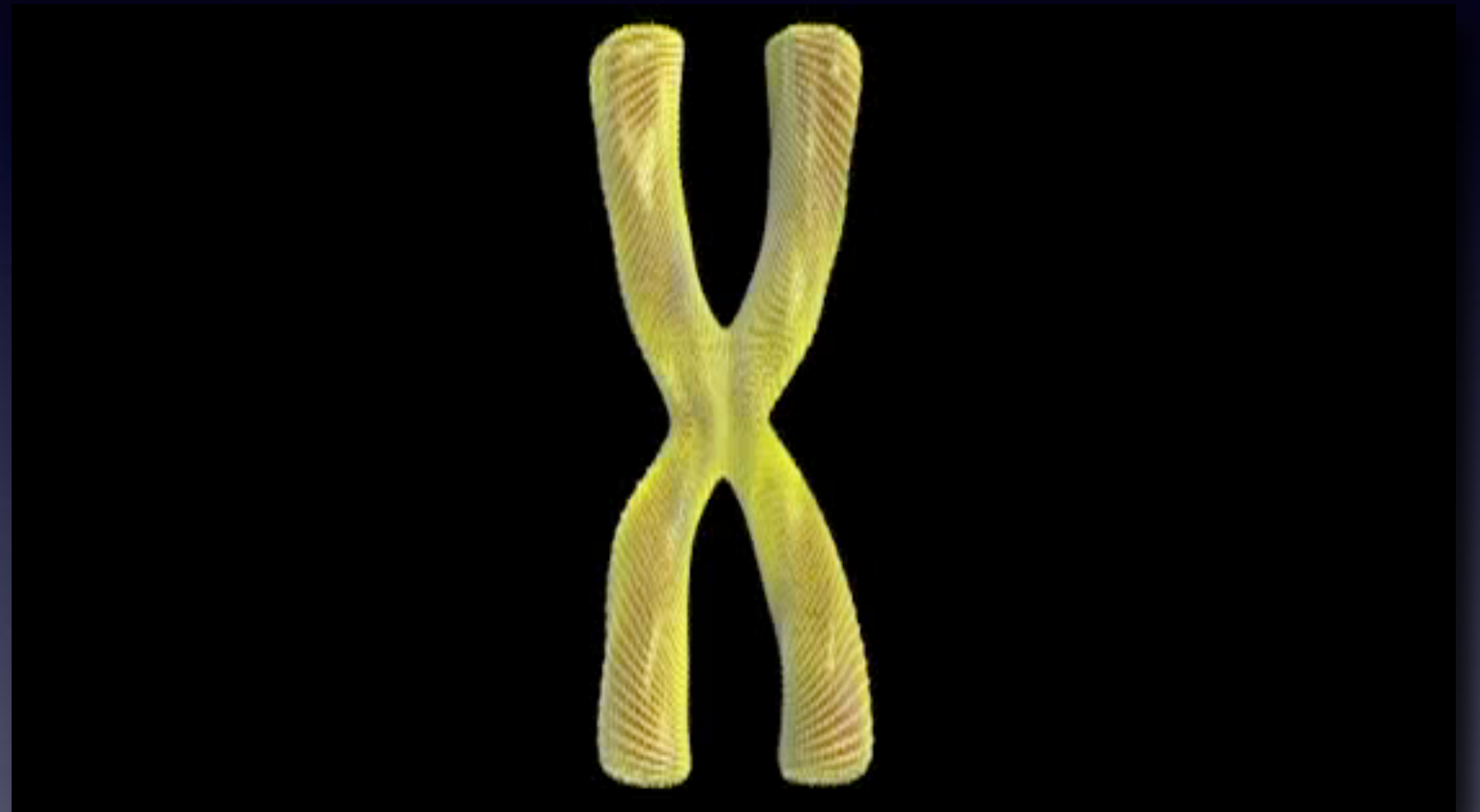
Chromosomes



Genes

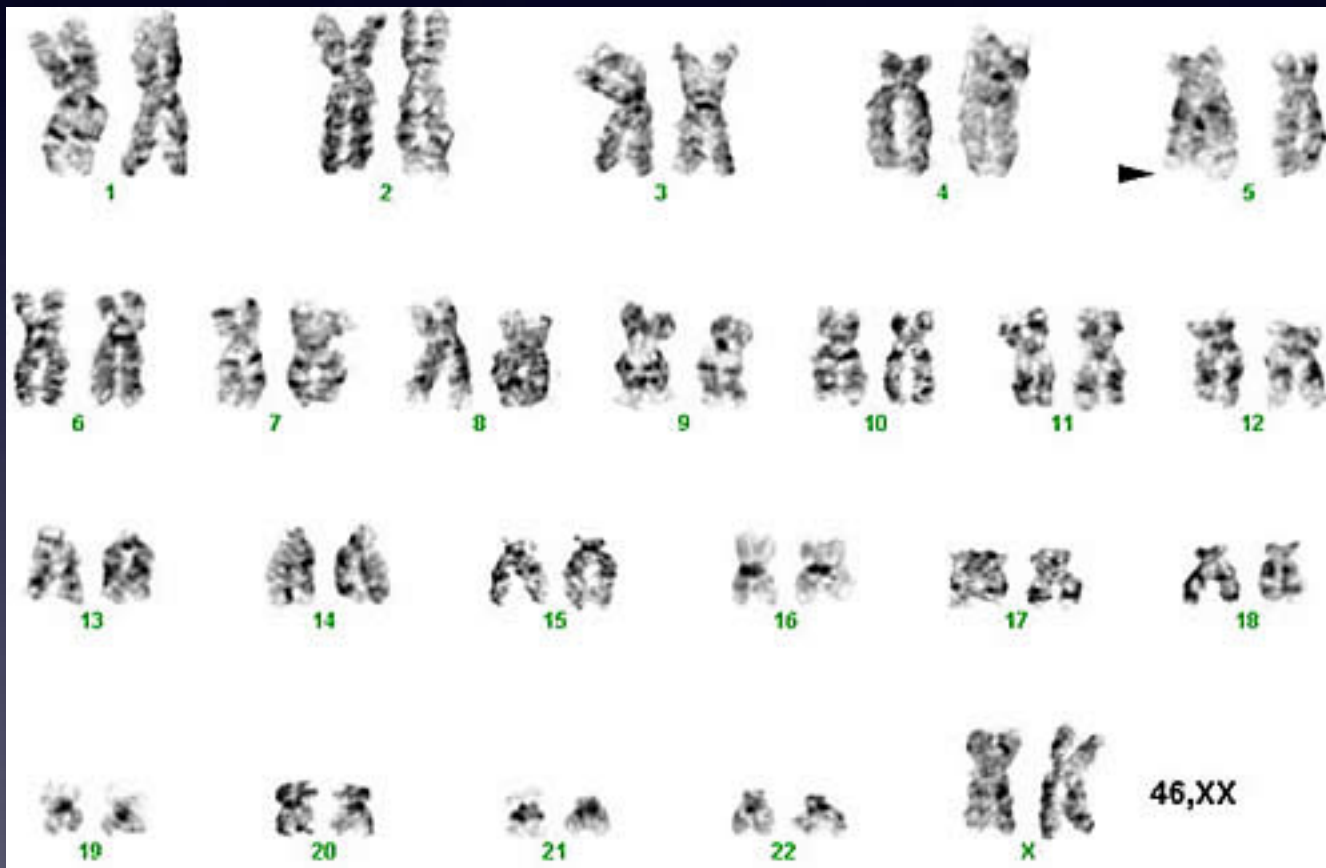


DNA



MDS Chromosomes

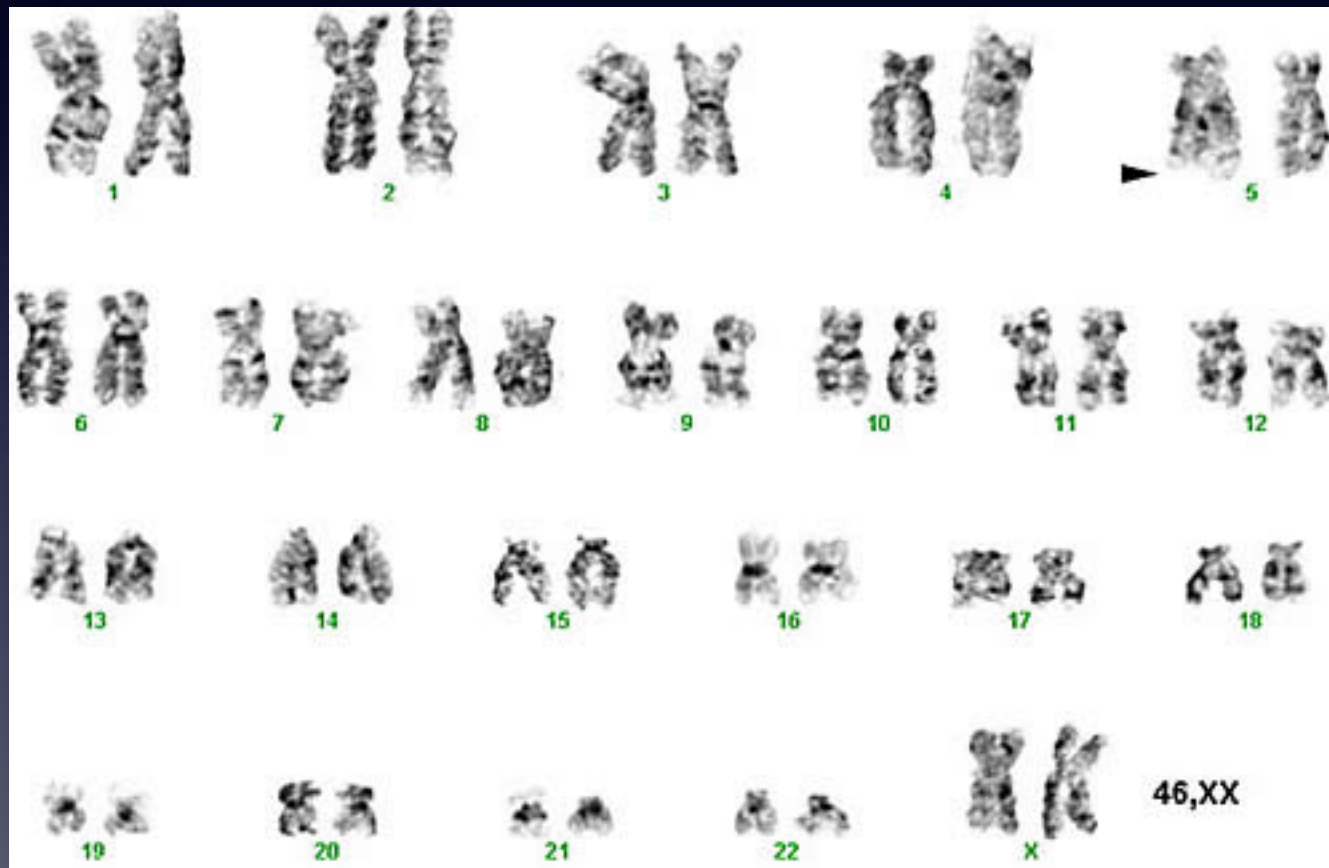
deletion 5q



lenalidomide (Revlimid)

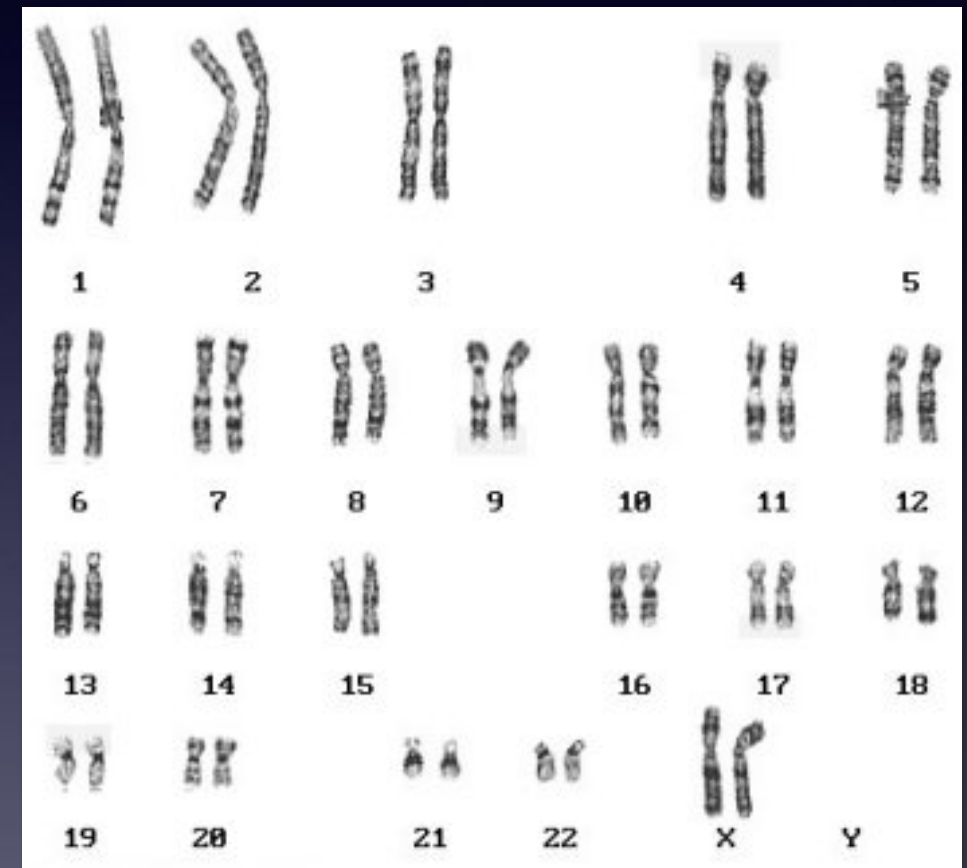
MDS Chromosomes

deletion 5q



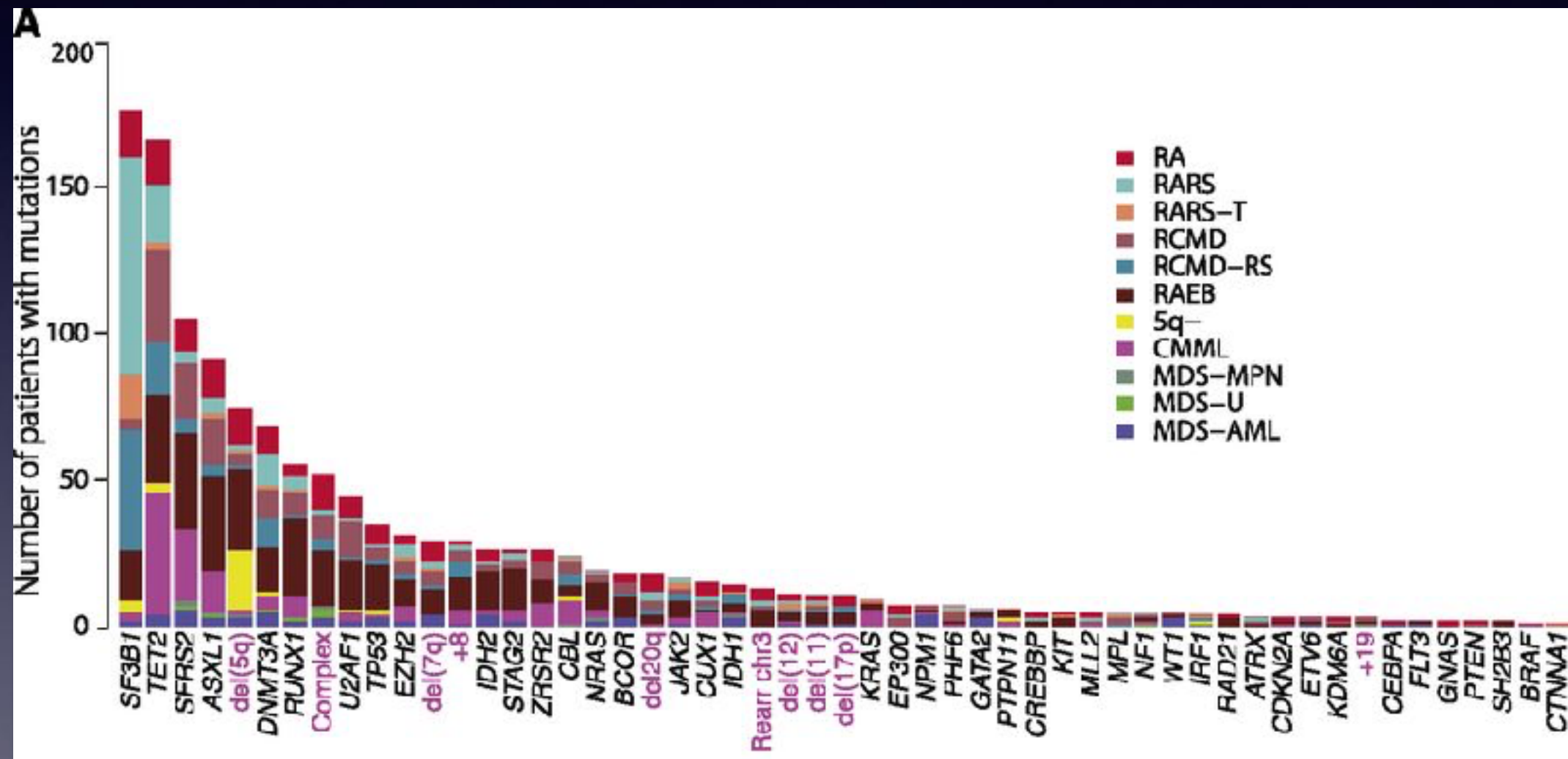
lenalidomide (Revlimid)

“normal”

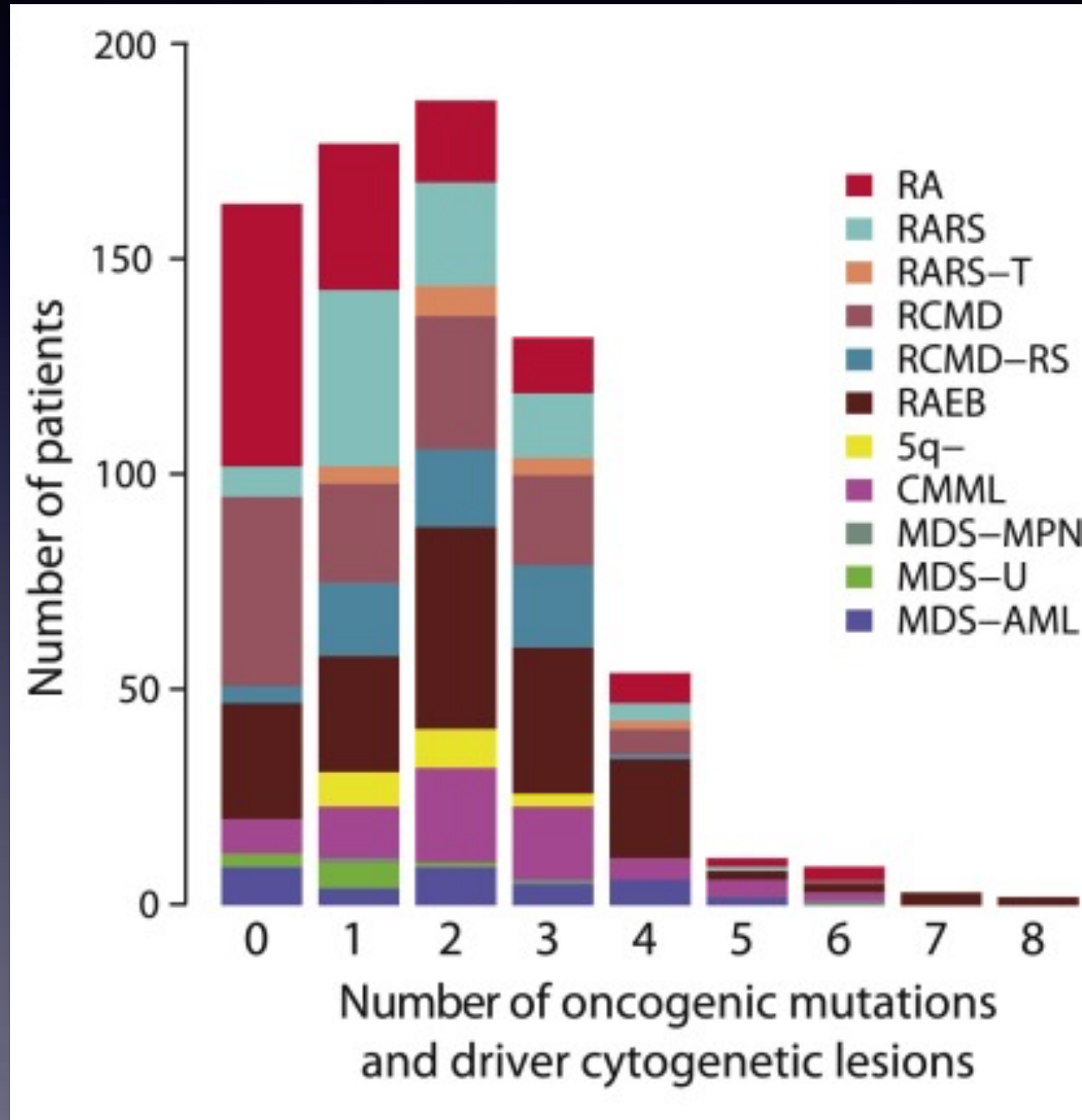


50% of MDS patients

MDS Gene Mutations



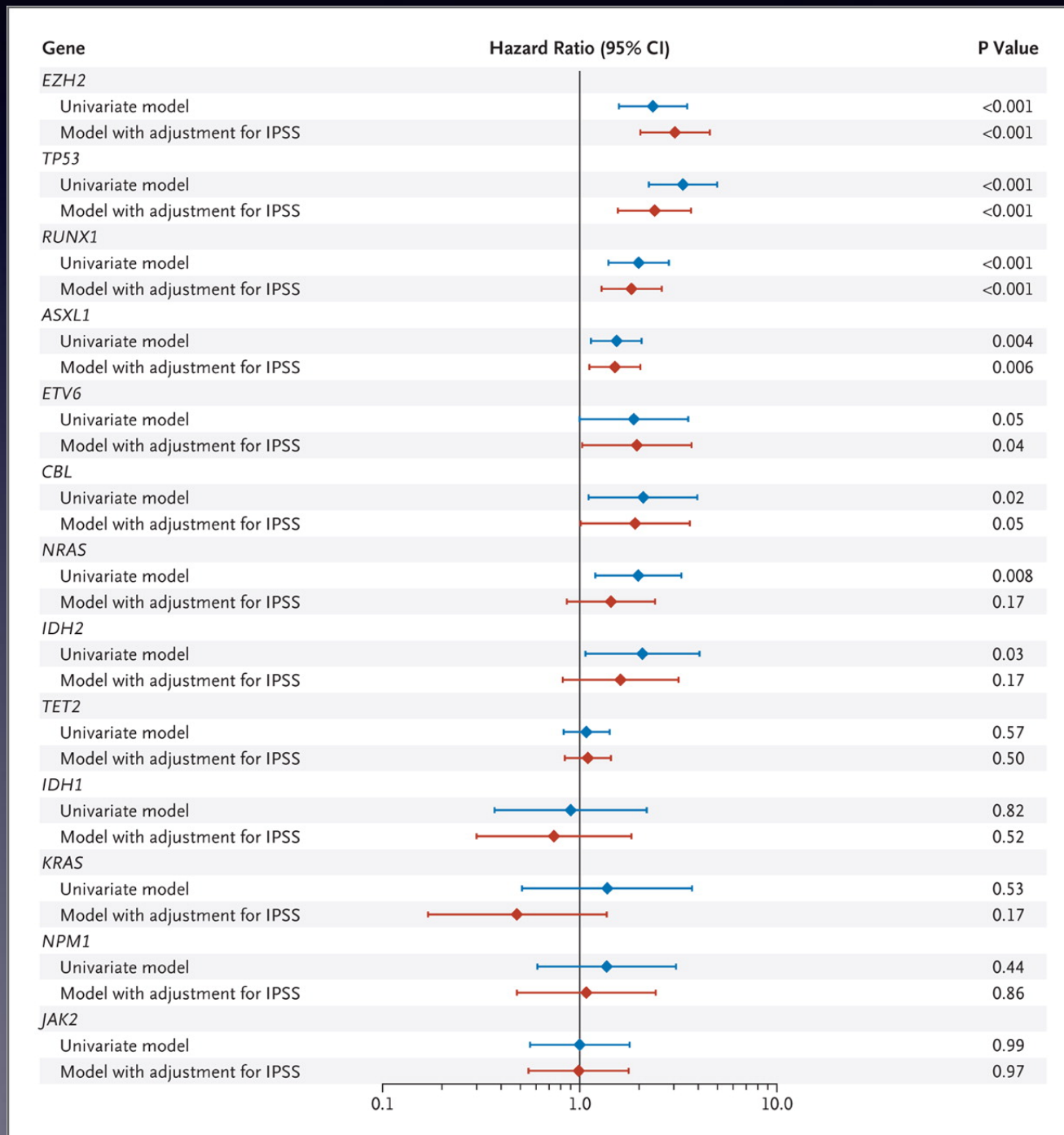
MDS Gene Mutations



78% of patients had at least 1 gene or chromosome abnormality

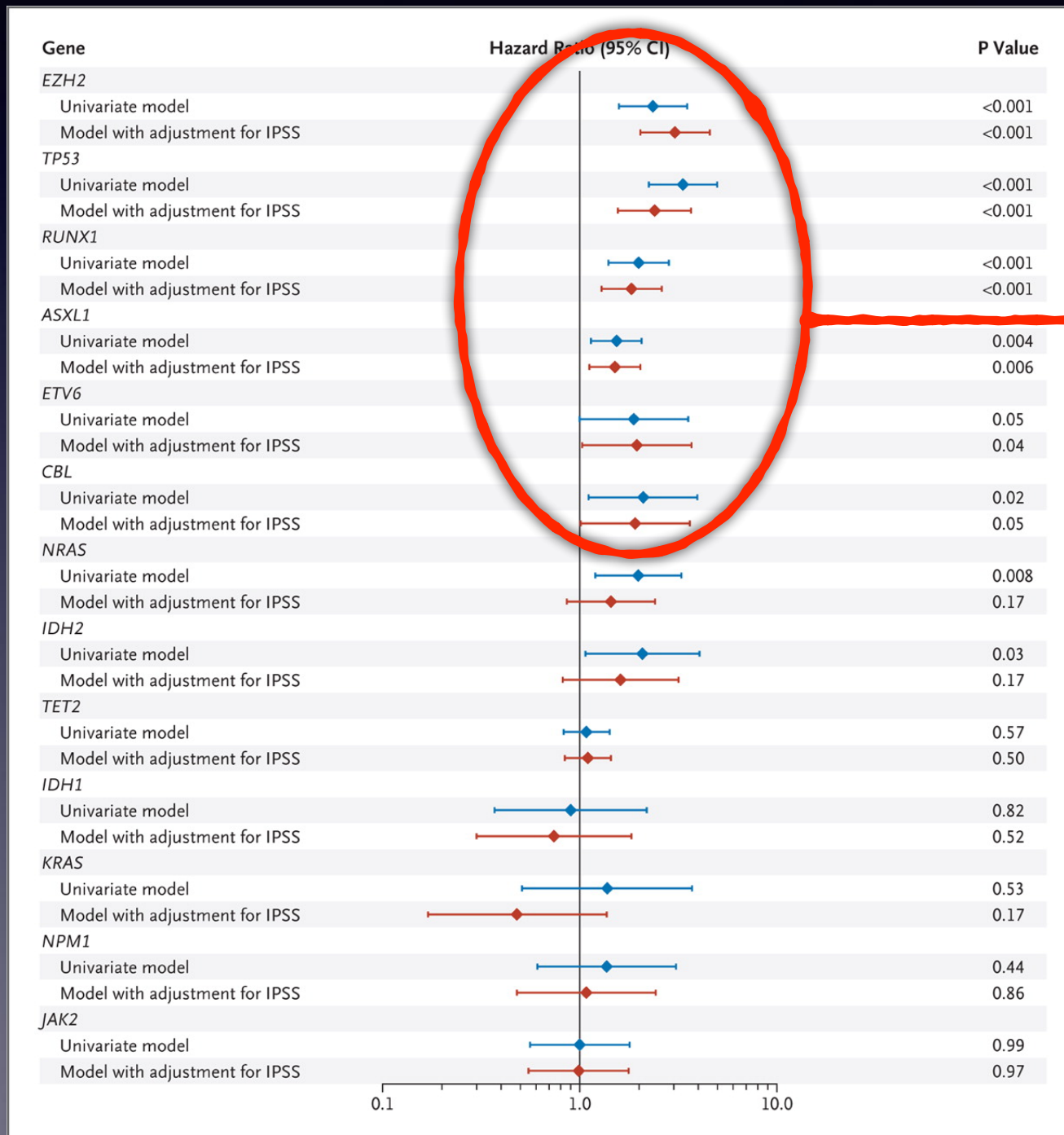
MDS Gene Mutations

Risk of Death and Progression to AML



MDS Gene Mutations

Risk of Death and Progression to AML



TP53
EZH2
ETV6
RUNX1
ASXL1

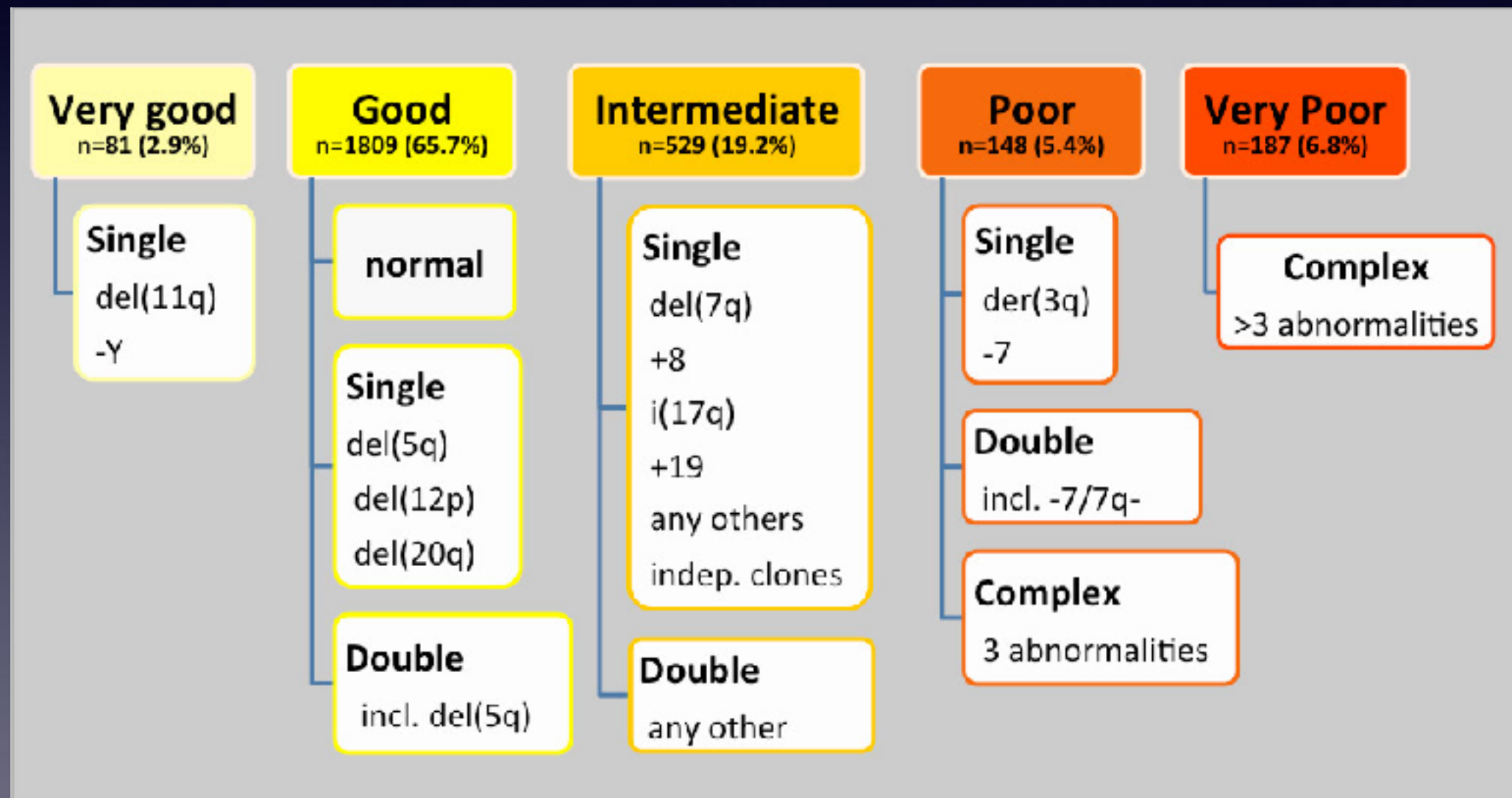
Current Thinking in MDS

IPSS-R Scoring System

Parameter	Categories and Associated Scores				
Cytogenetic risk group	Very good	Good	Intermediate	Poor	Very Poor
	0	1	2	3	4
Marrow blast proportion	≤2%	>2% to <5%	5% to 10%	>10%	
	0	1	2	3	
Hemoglobin	≥10 g/dL	8 to <10 g/dL	<8 g/dL		
	0	1	1.5		
Absolute neutrophil count	≥0.8 × 10 ⁹ /L	<0.8 × 10 ⁹ /L			
	0	0.5			
Platelet count	≥100 × 10 ⁹ /L	50 to <100 × 10 ⁹ /L	<50 × 10 ⁹ /L		
	0	0.5	1		

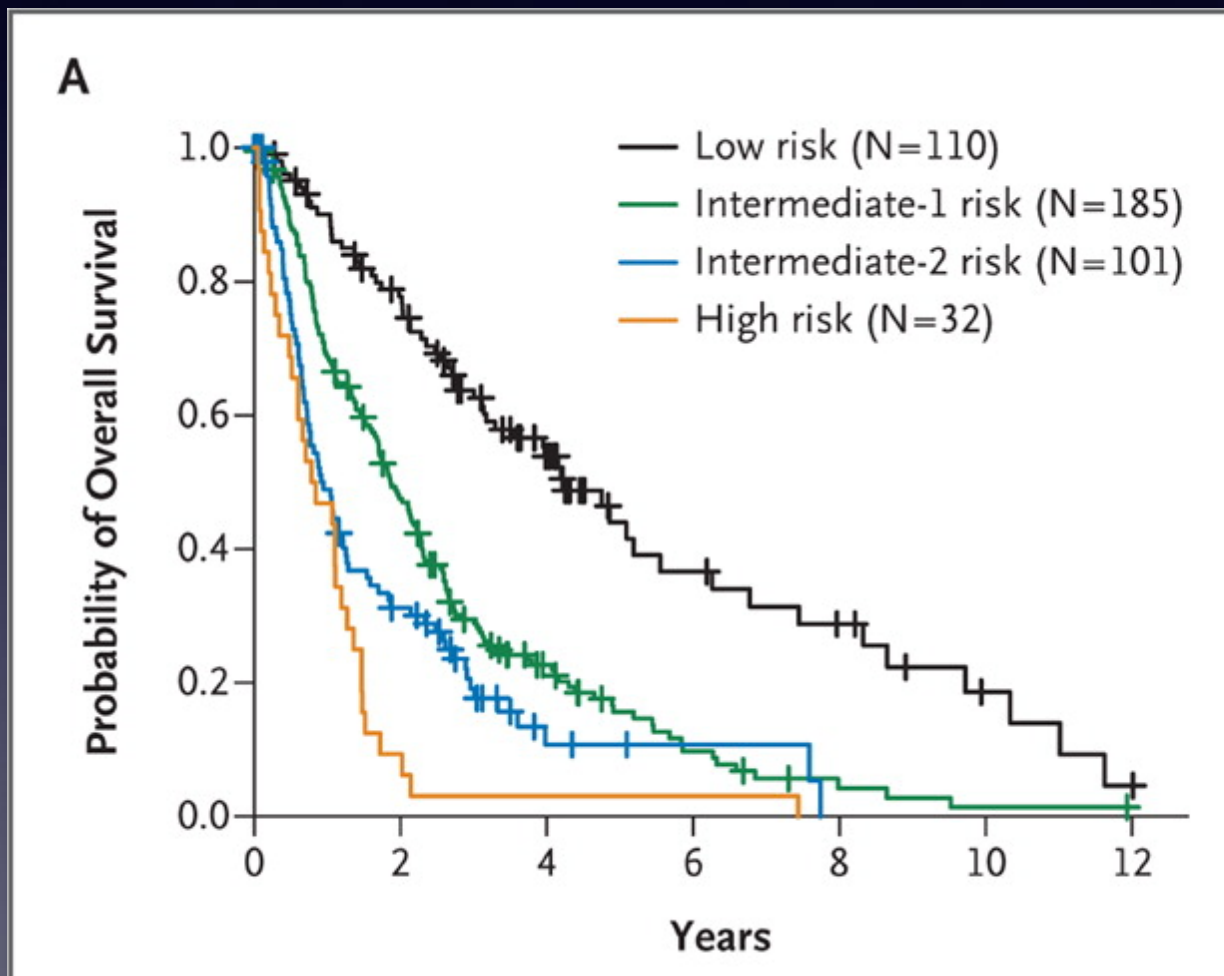
Current Thinking in MDS

IPSS-R Chromosome Scoring



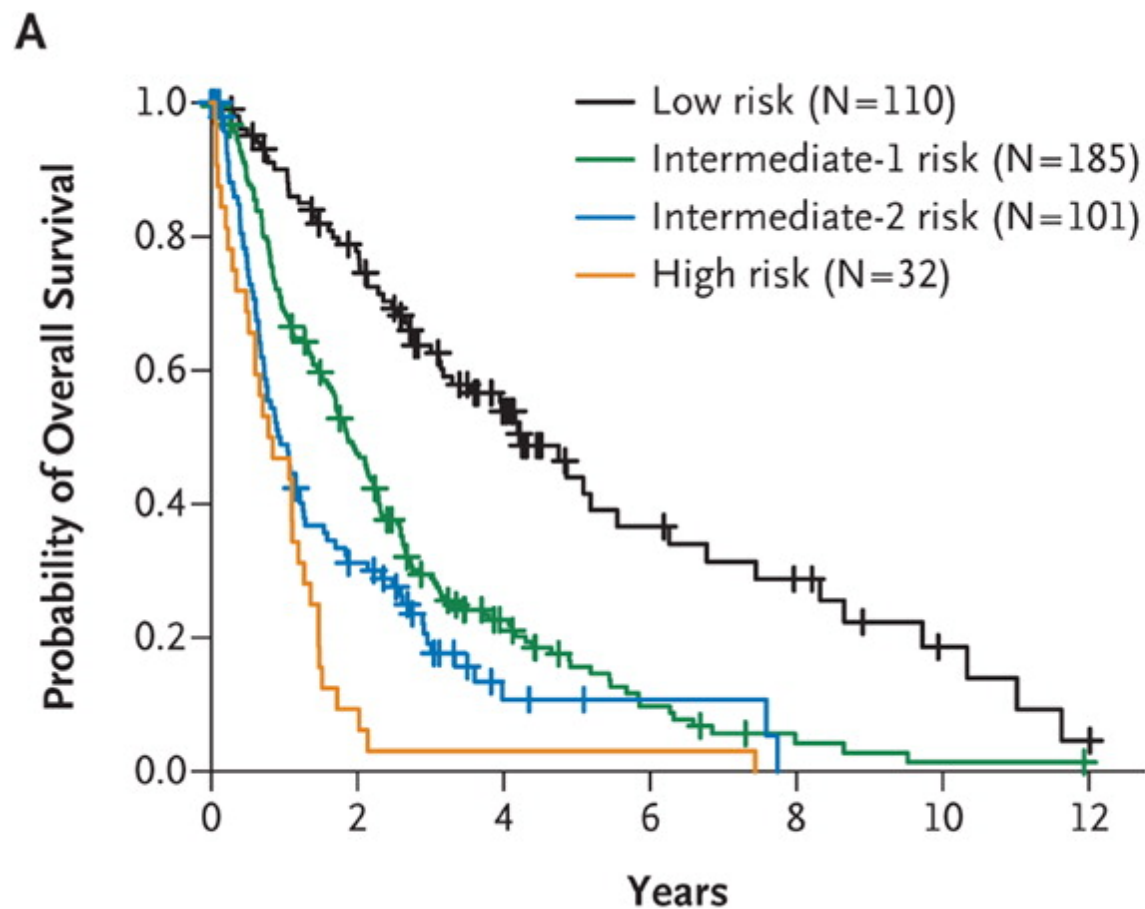
MDS Gene Mutations

Old News

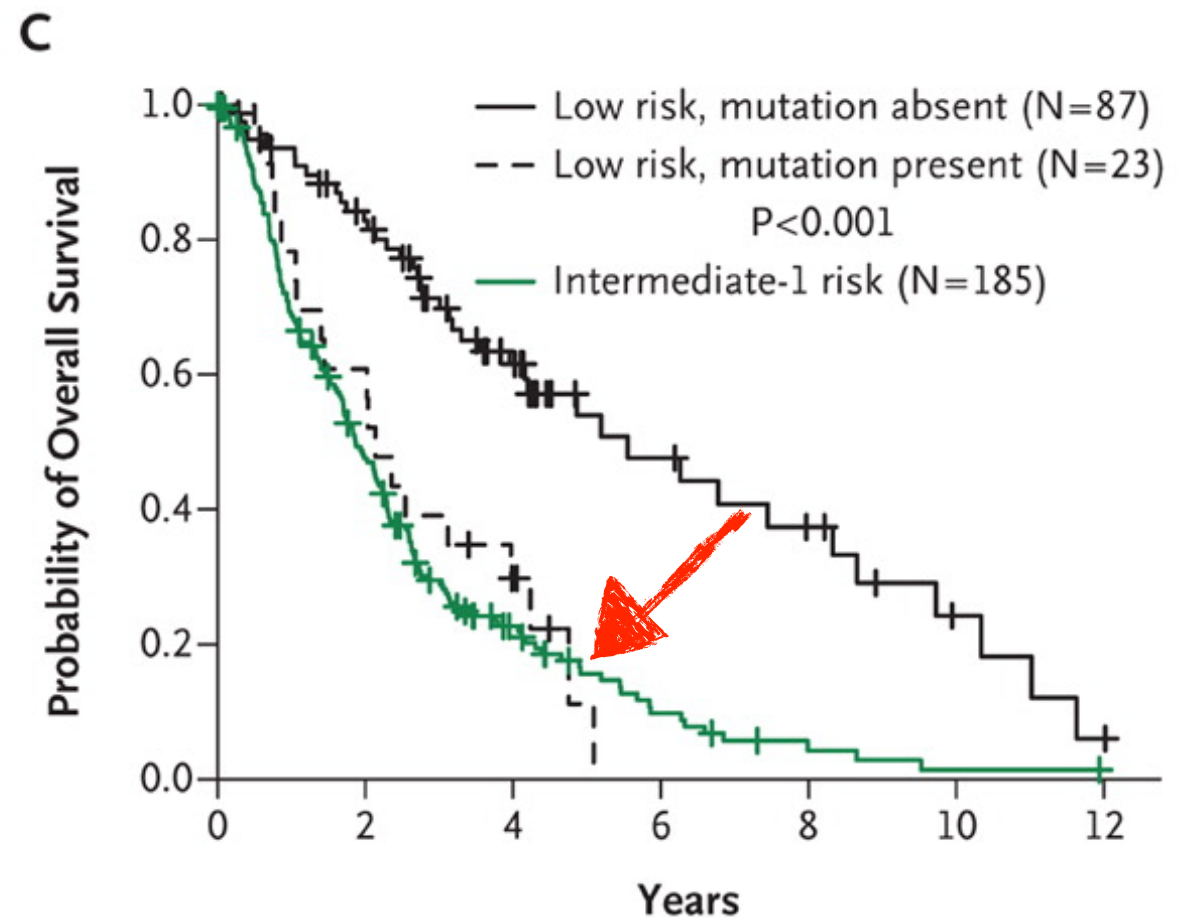


MDS Gene Mutations

Old News

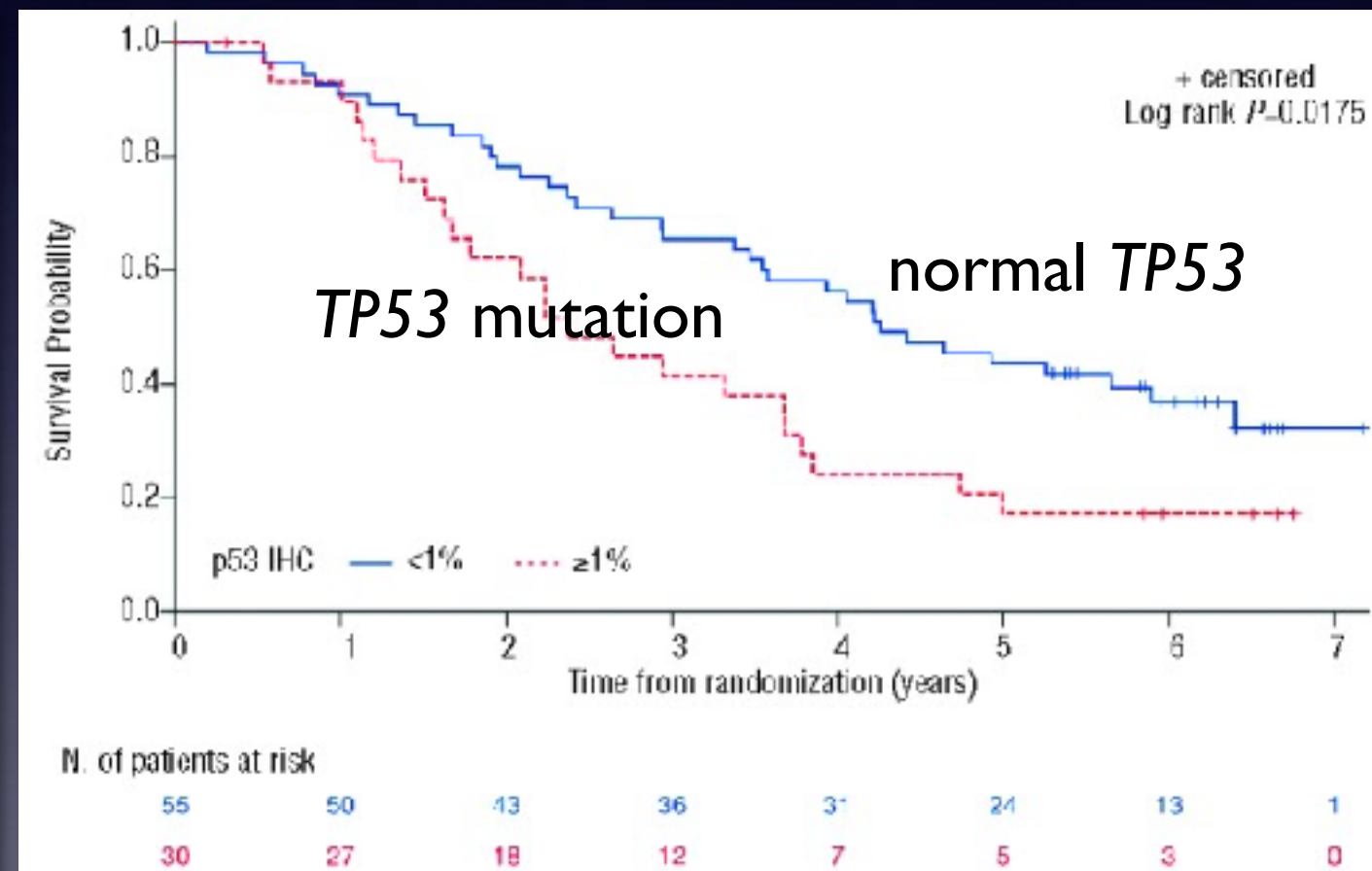
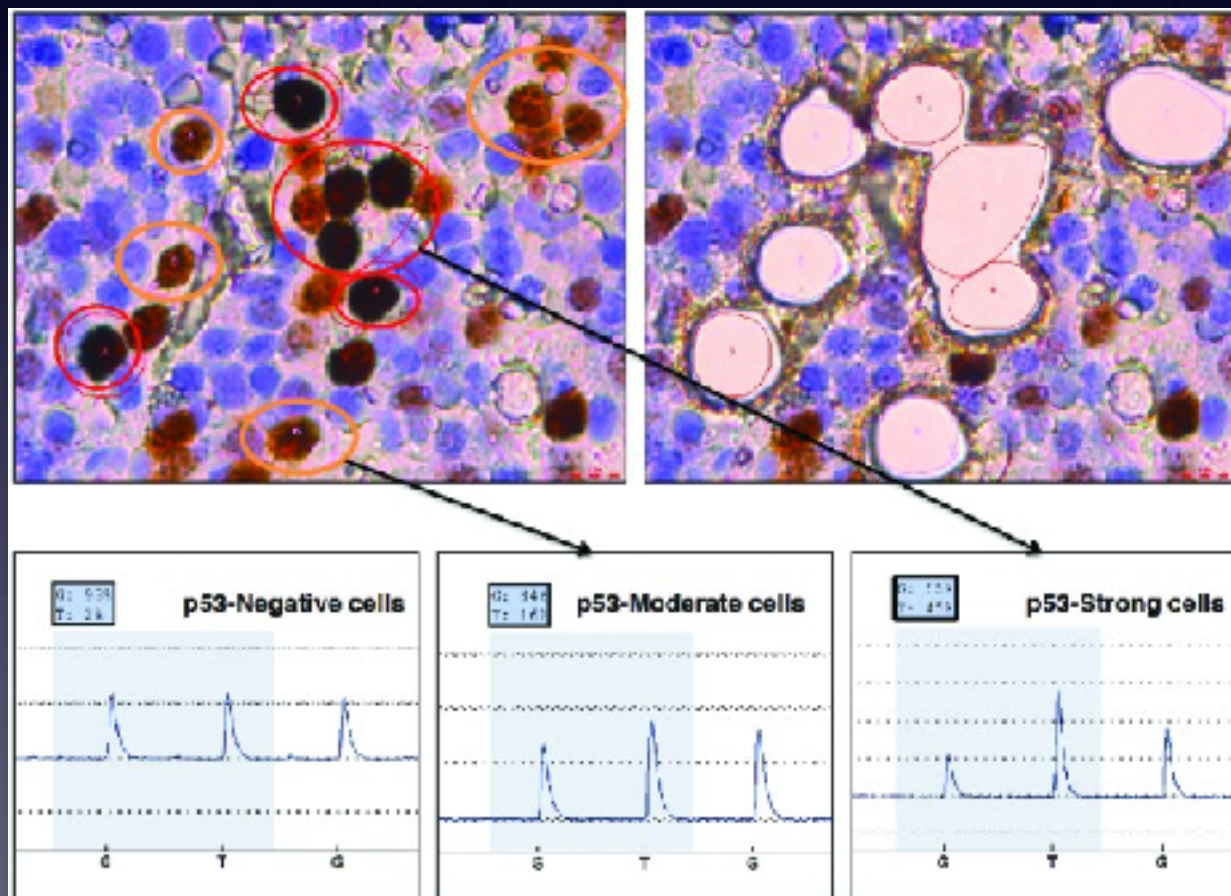


New News



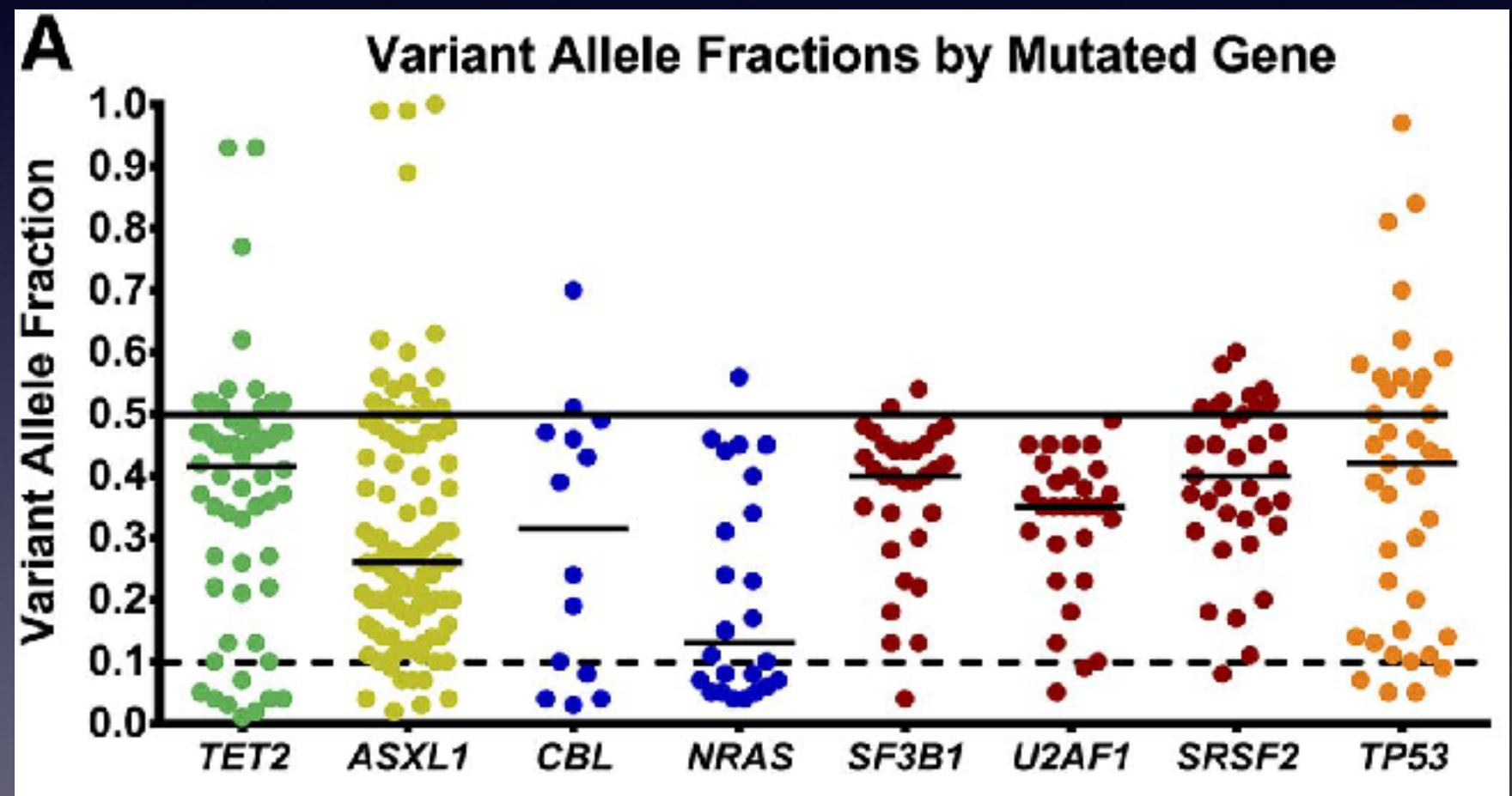
MDS Gene Mutations

Response to Lenalidomide



MDS Gene Mutations

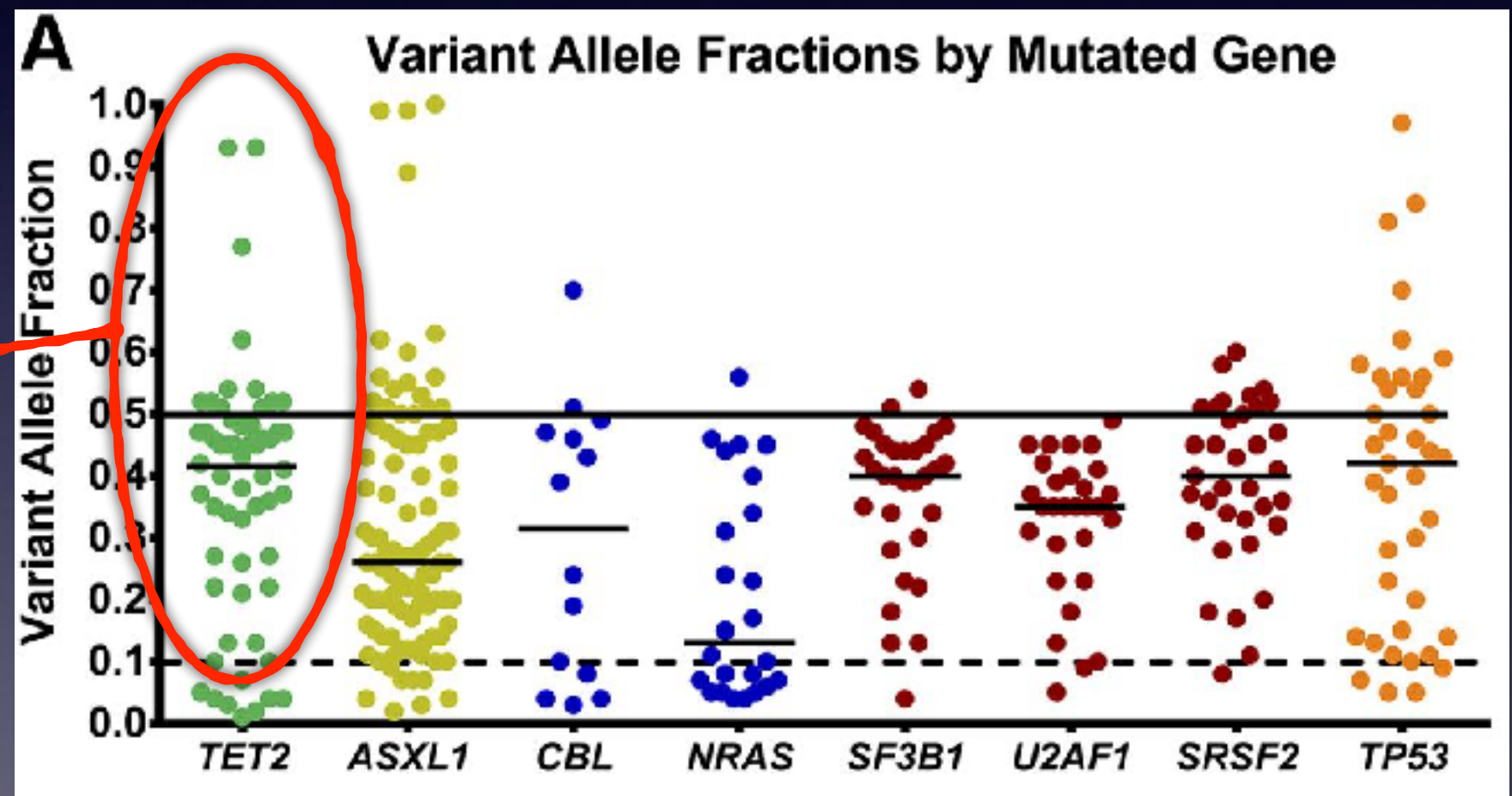
Response to Azacitidine



MDS Gene Mutations

Response to Azacitidine

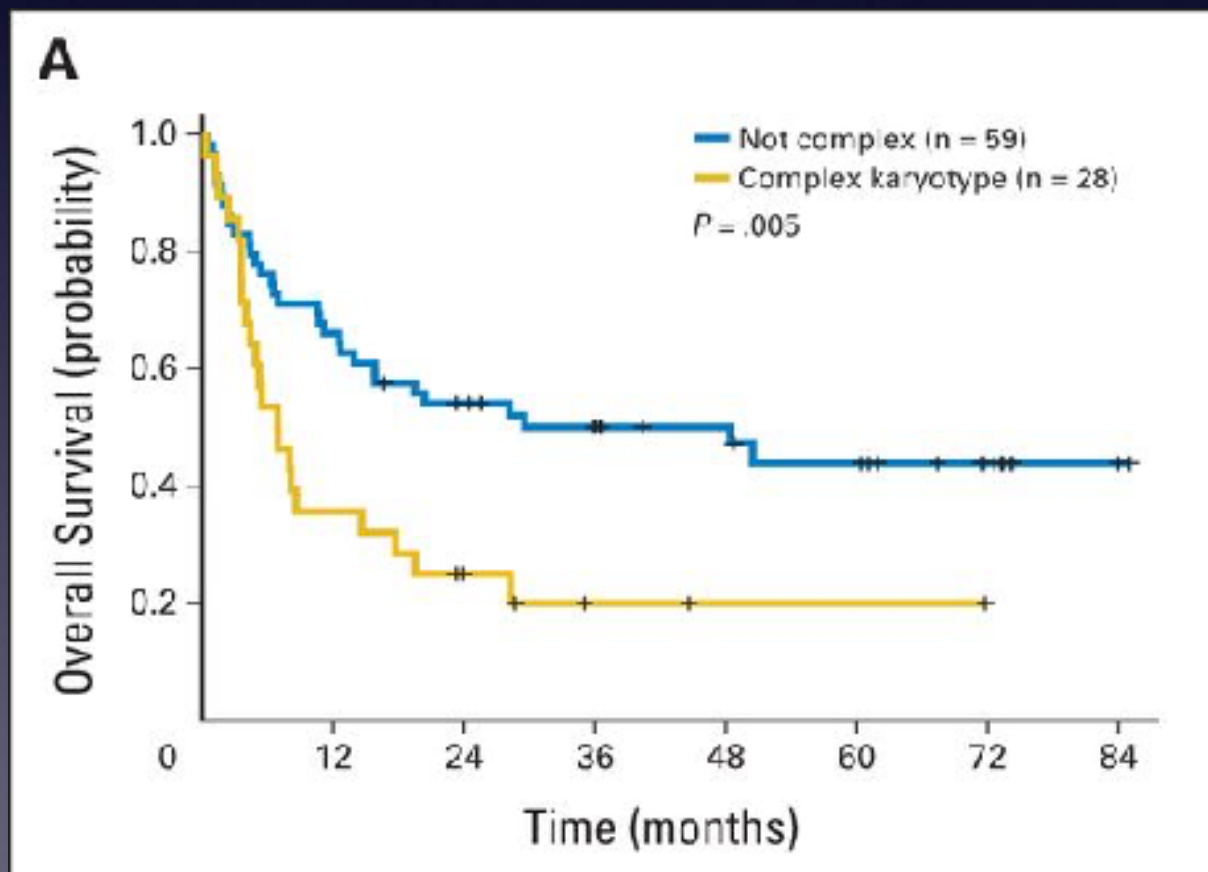
2 x more
likely to
achieve
response



MDS Gene Mutations

Response to Transplant

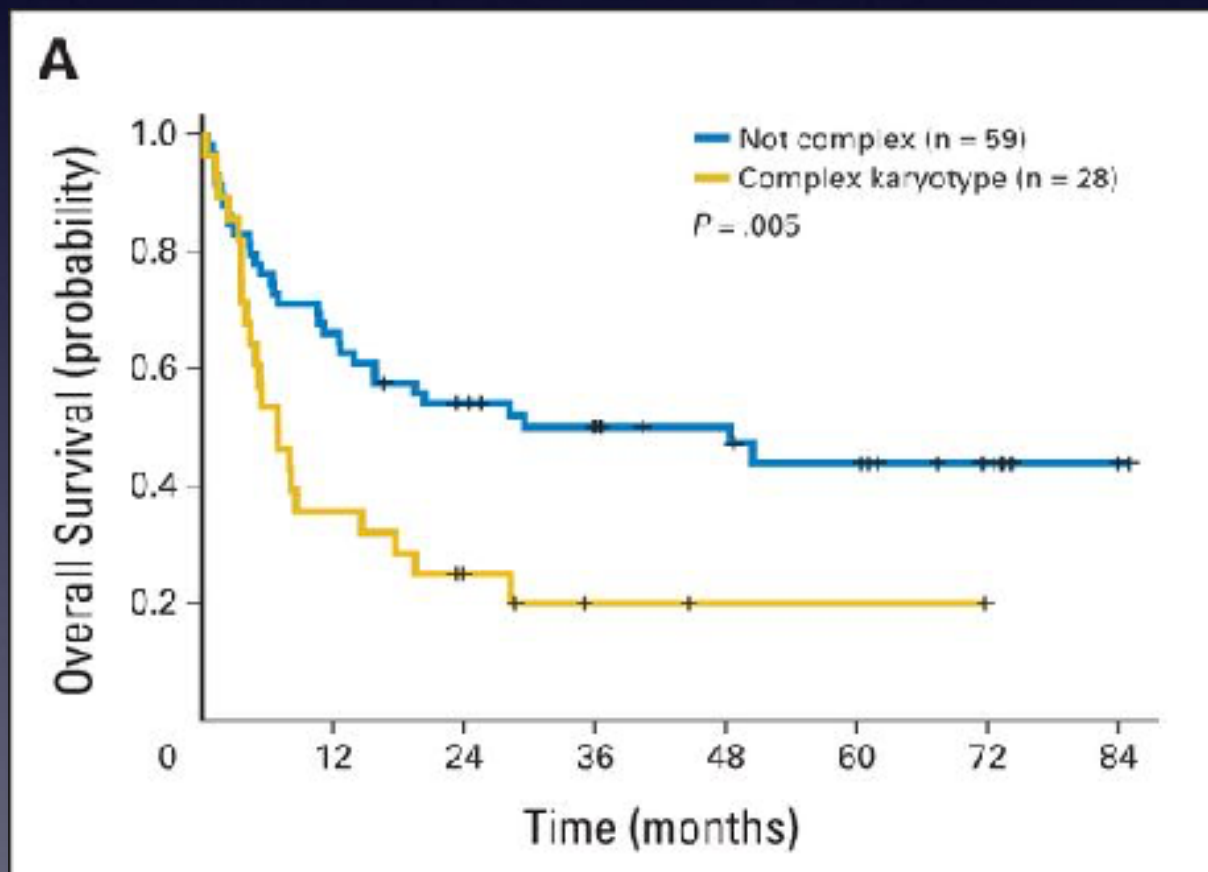
Old News



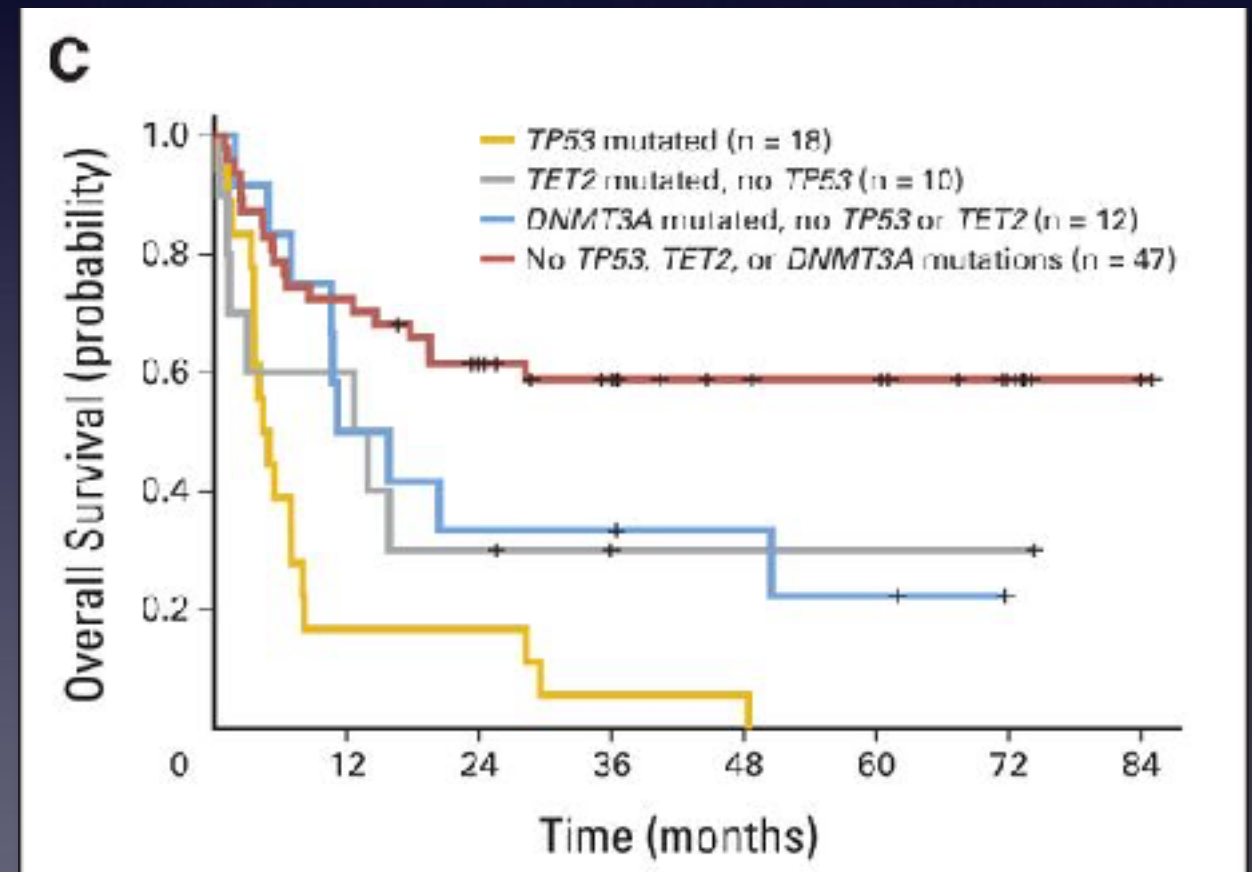
MDS Gene Mutations

Response to Transplant

Old News



New News



Current Thinking in MDS



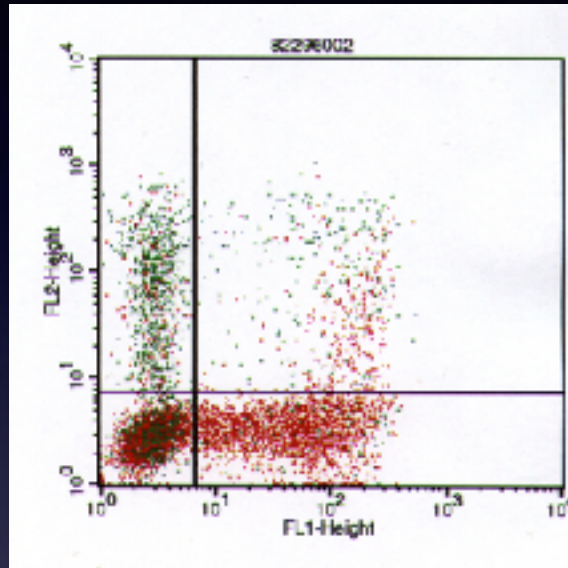
Current Thinking in MDS



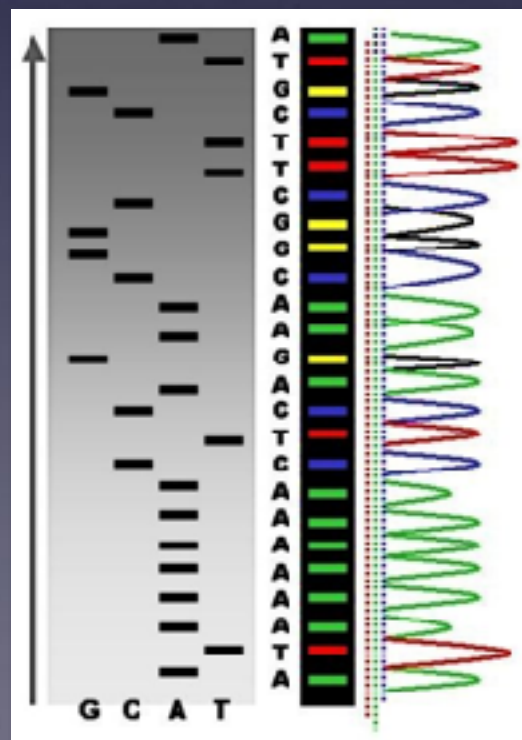
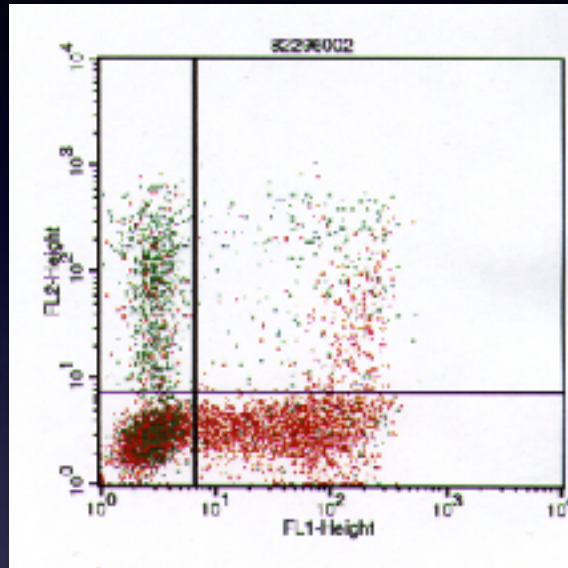
Current Thinking in MDS



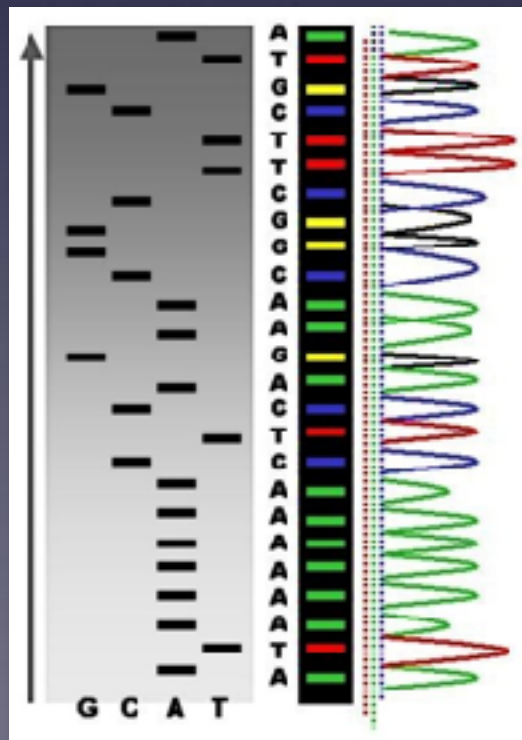
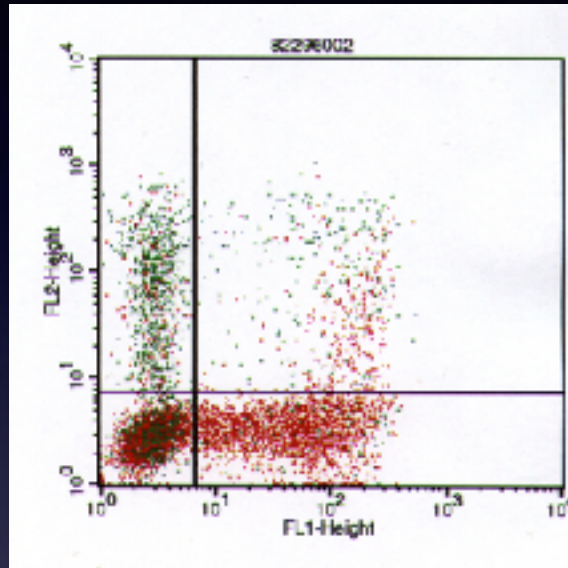
Current Thinking in MDS



Current Thinking in MDS

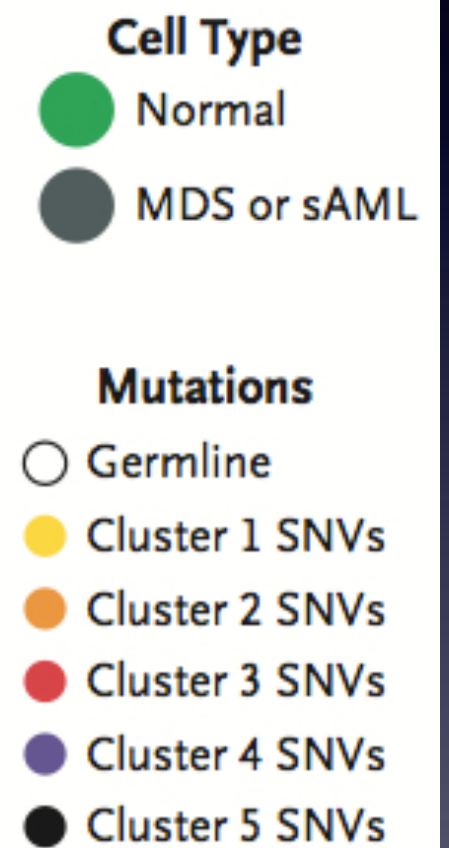
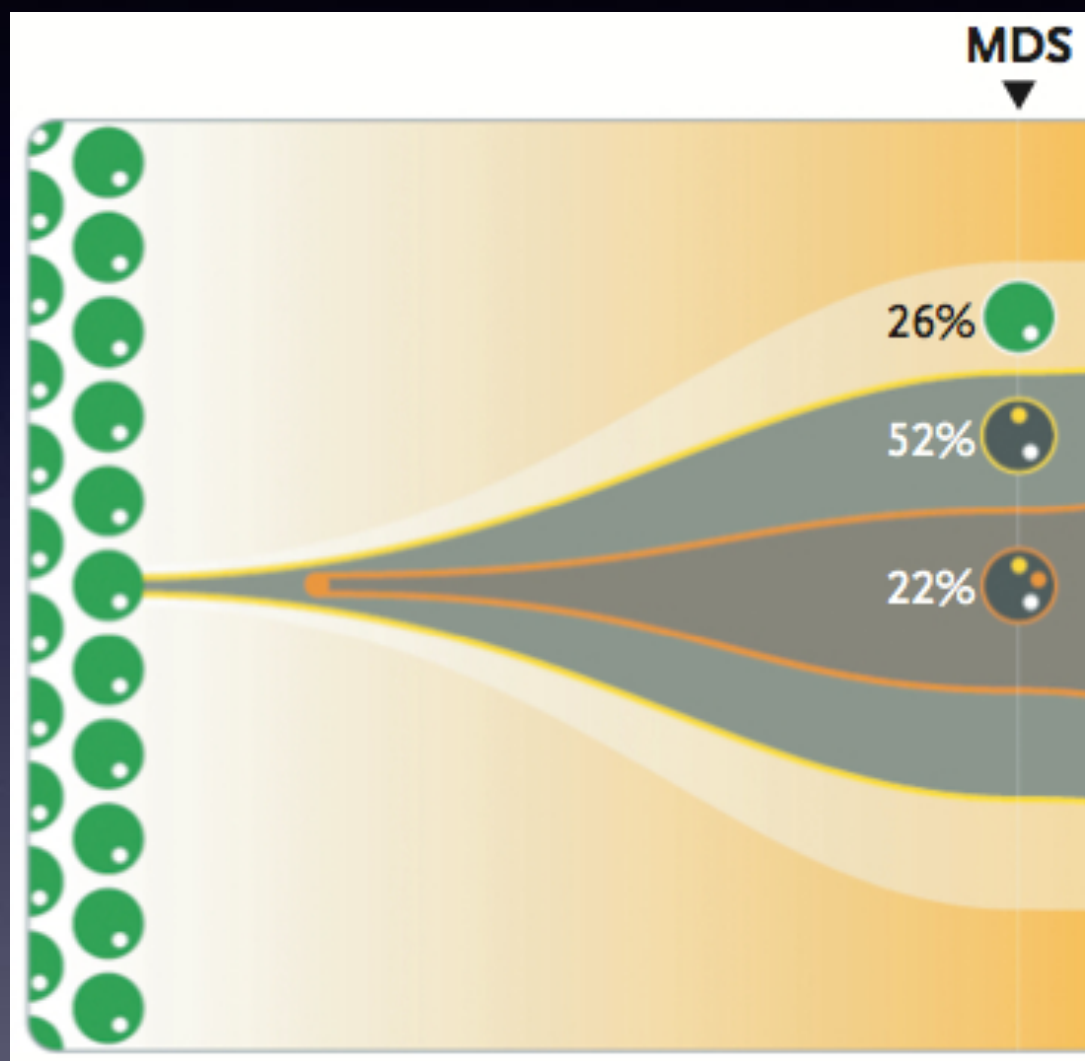


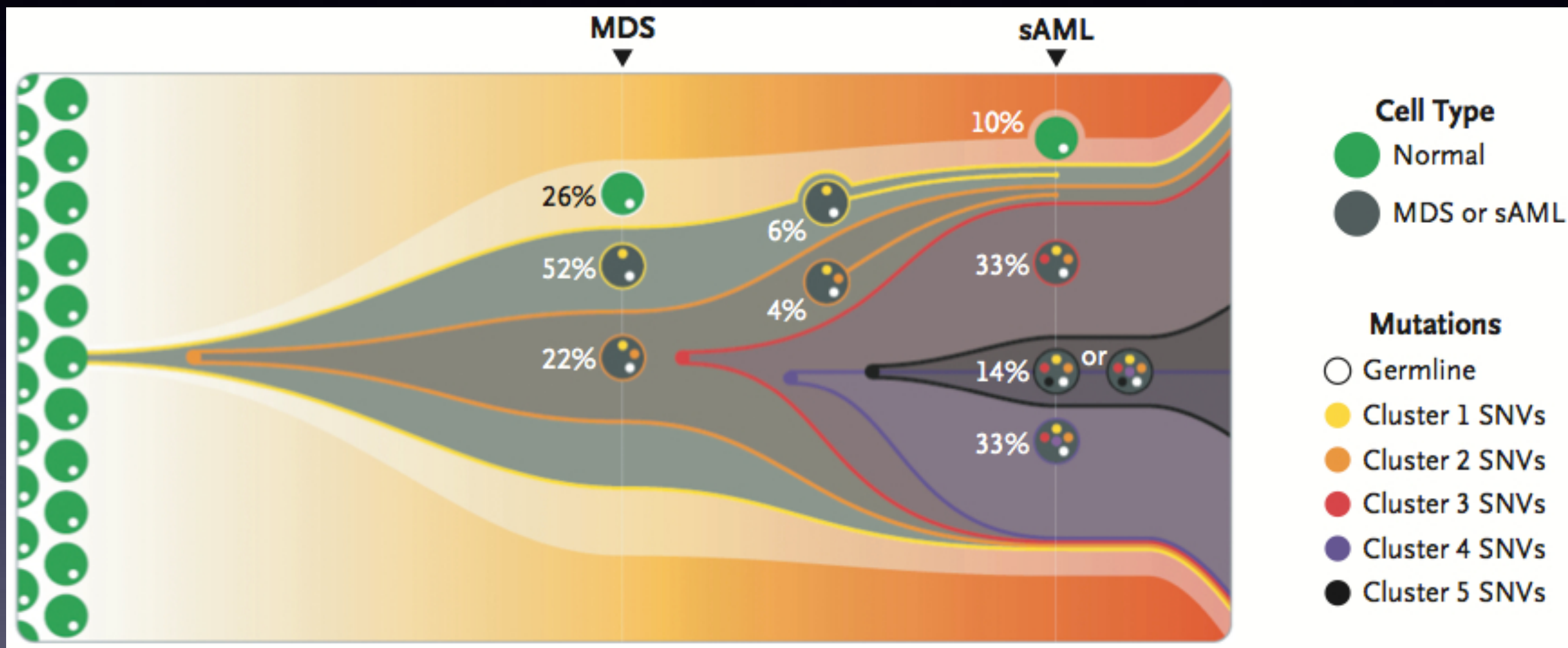
Current Thinking in MDS

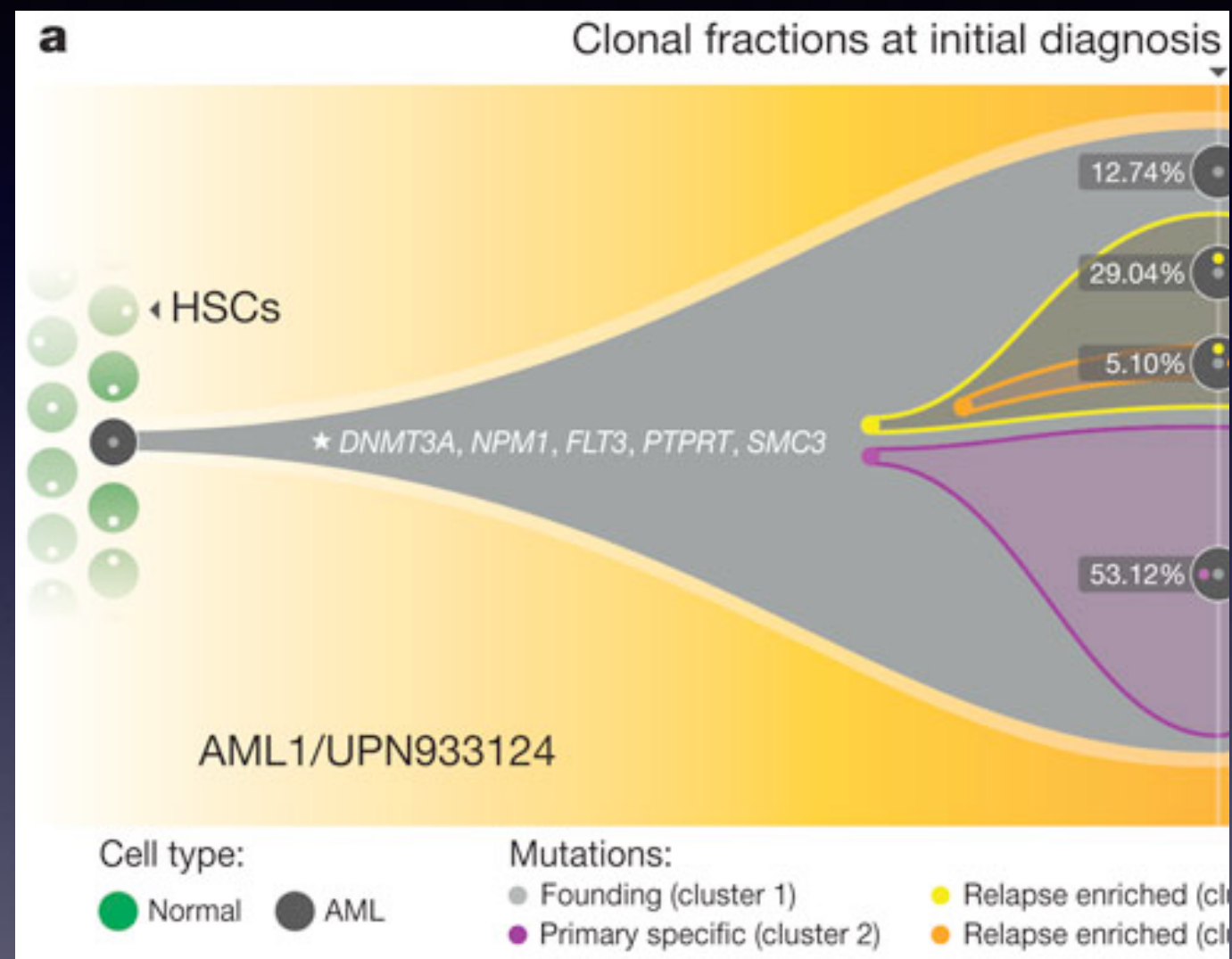


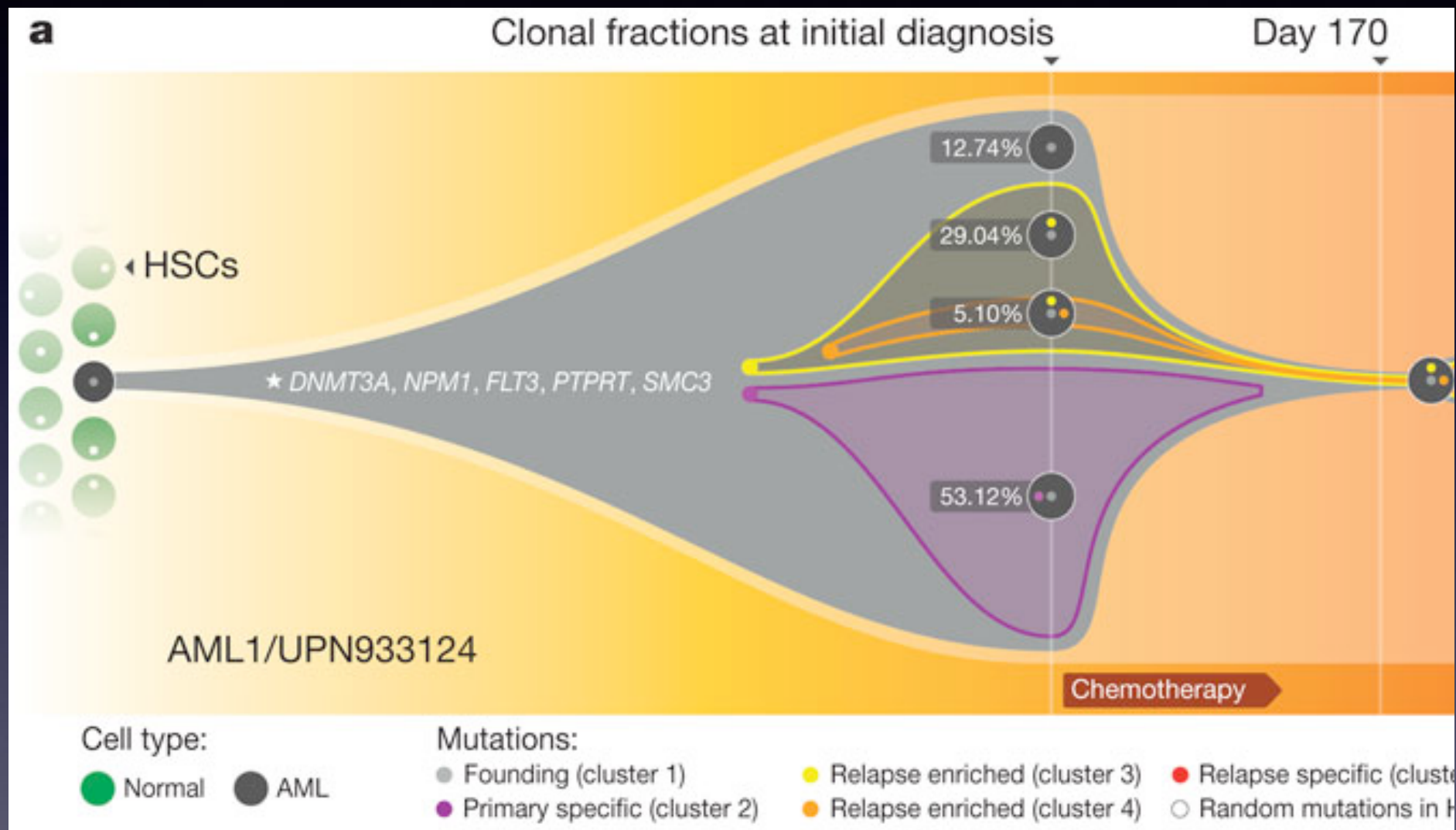
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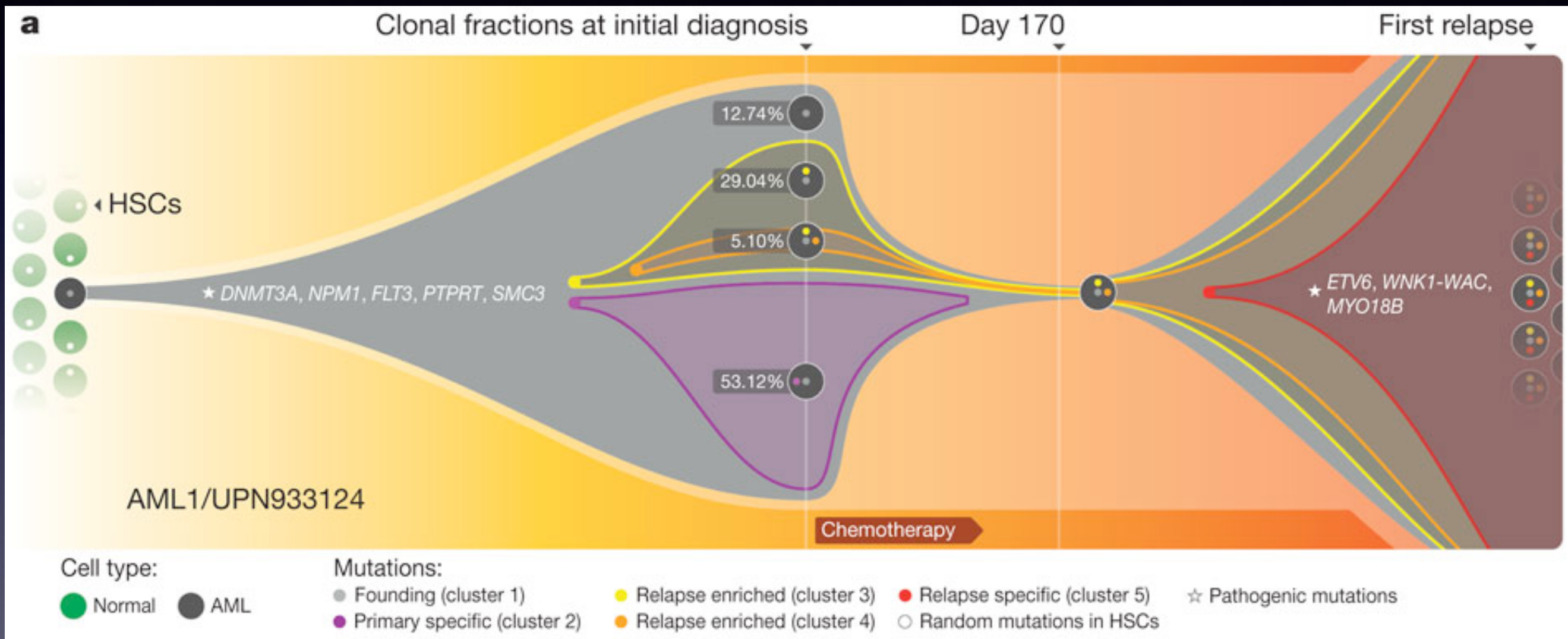
Clone Wars







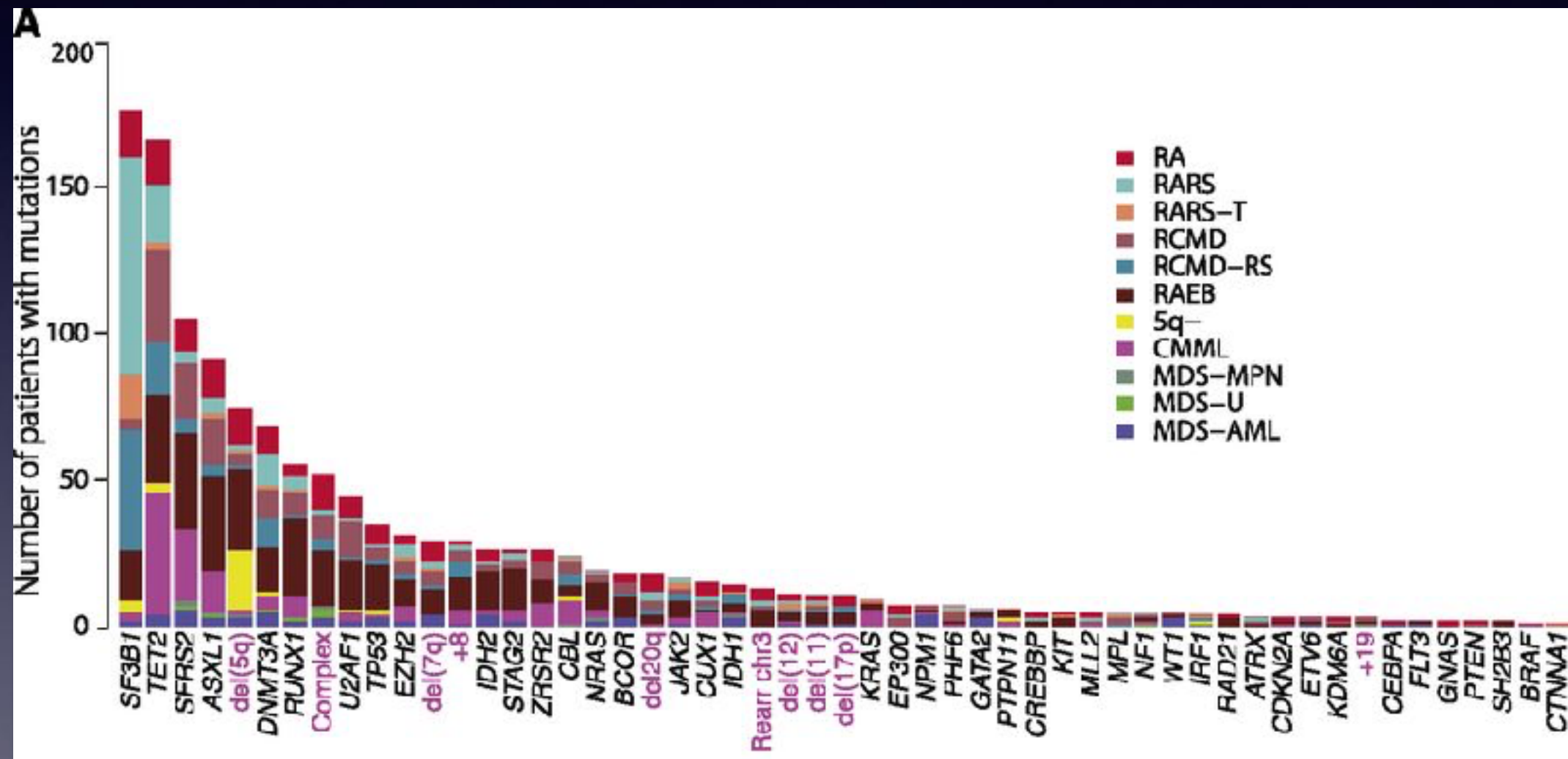




4

Quiet Beginnings

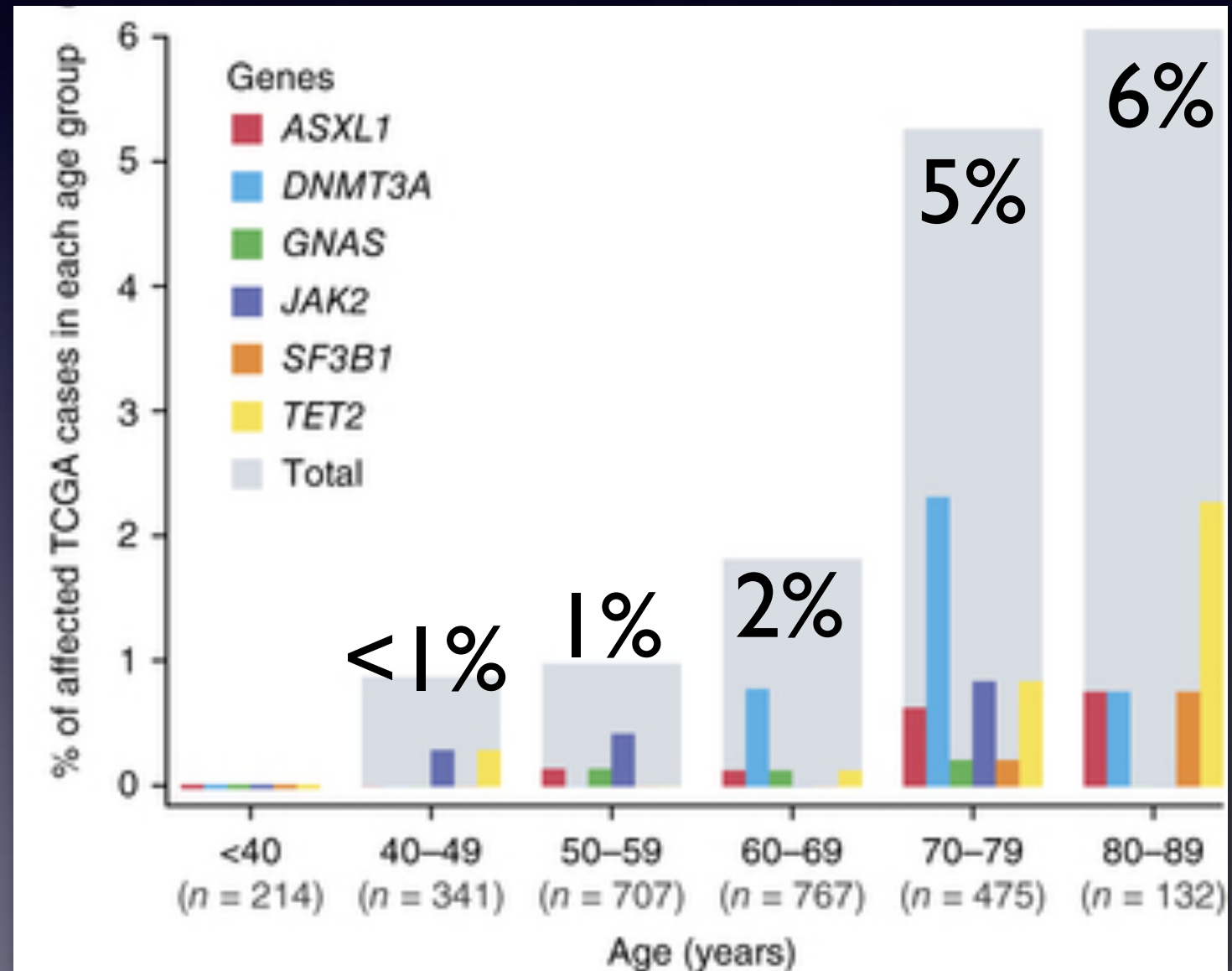
MDS Gene Mutations



MDS Gene Mutations in the General Population



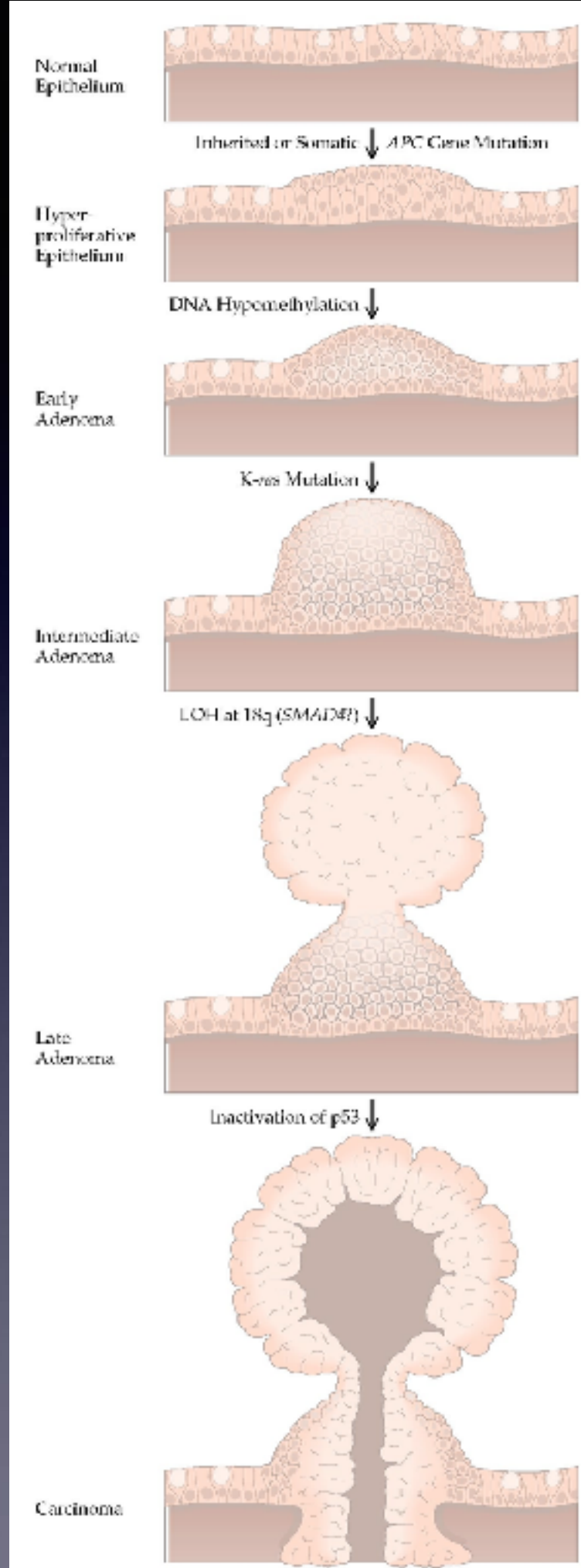
MDS Gene Mutations in the General Population



Normal Tissue



Cancer Tissue



Normal Tissue



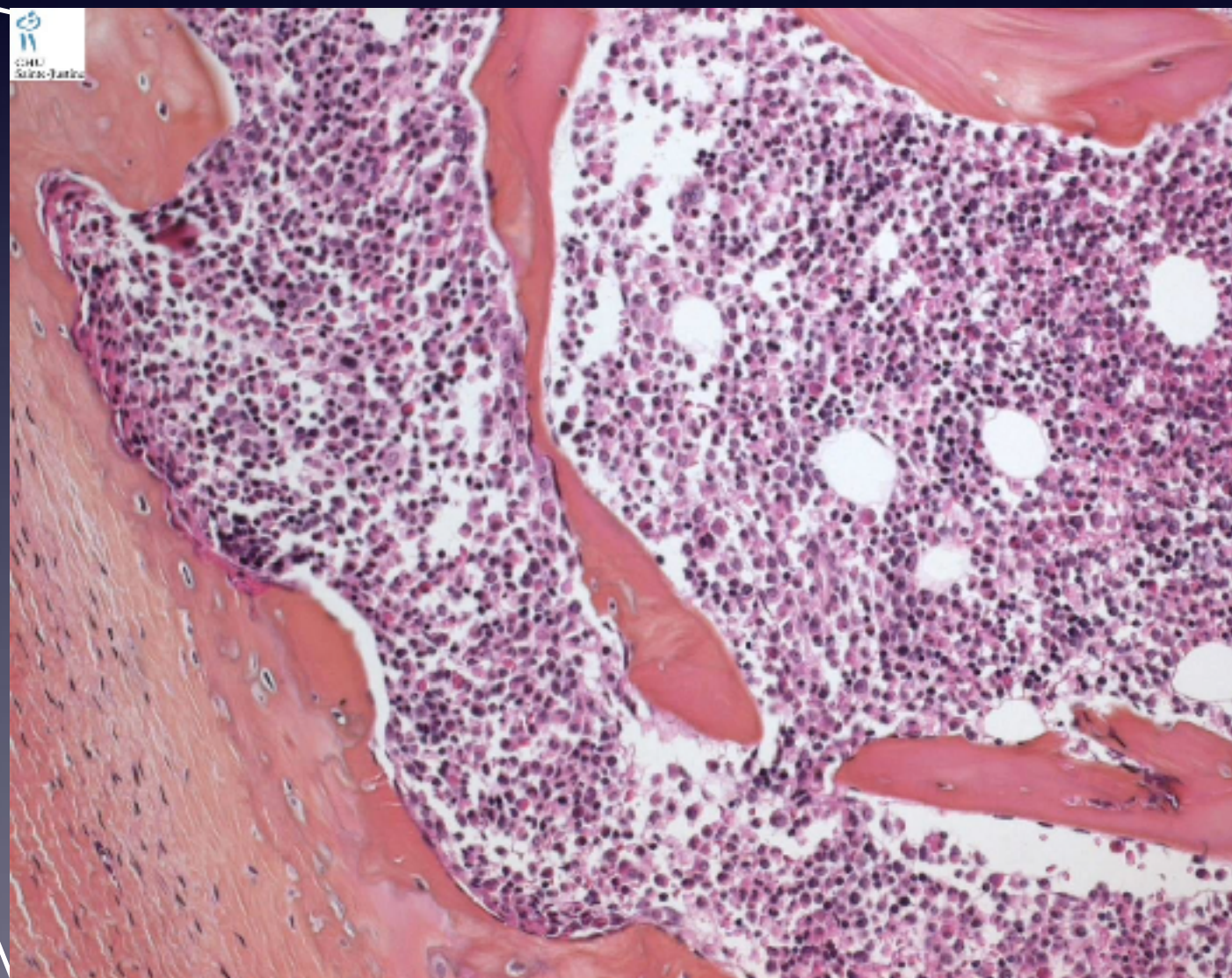
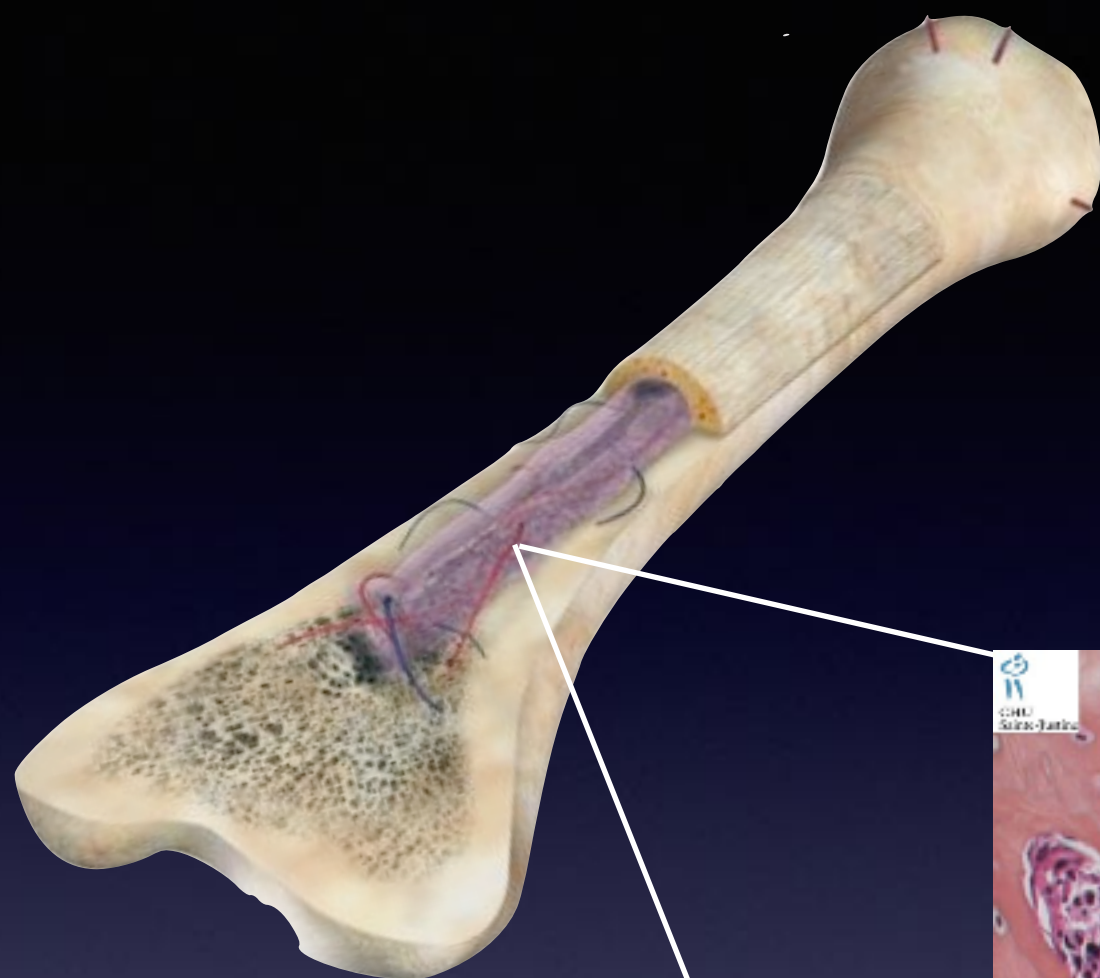
Cancer Tissue

Multi-Hit Hypothesis



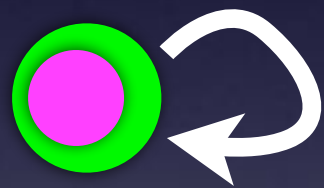
5

Absentee Parenting



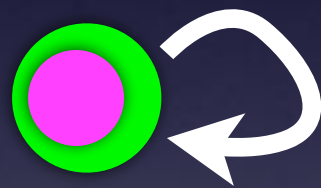
Hematopoietic Stem Cell

Hematopoietic Stem Cell

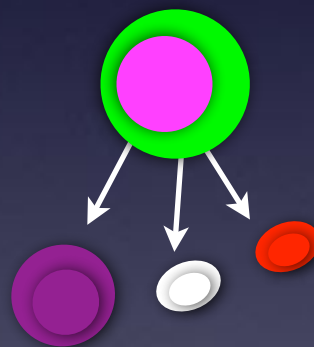


Self Renewal

Hematopoietic Stem Cell

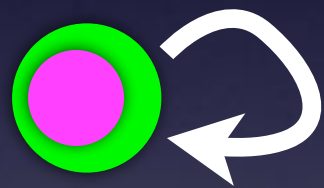


Self Renewal

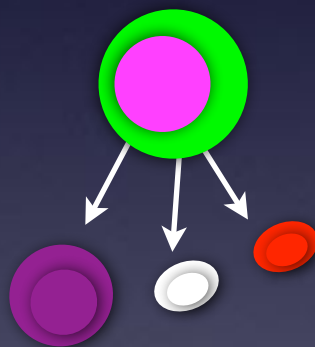


Multi-Lineage
Differentiation

Hematopoietic Stem Cell



Self Renewal

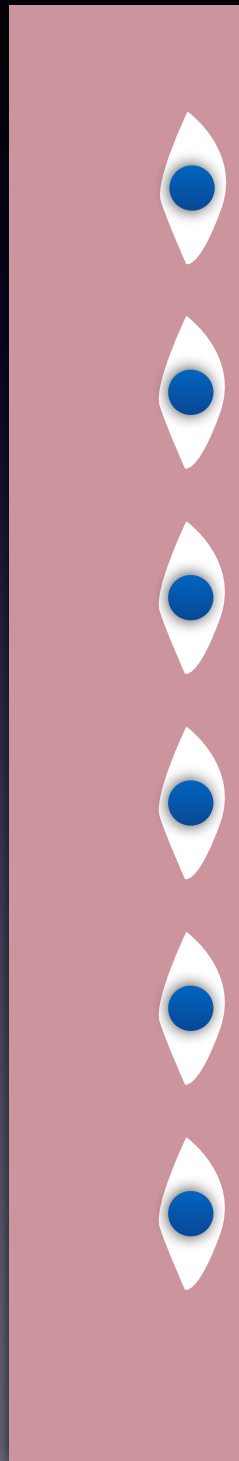


Multi-Lineage
Differentiation

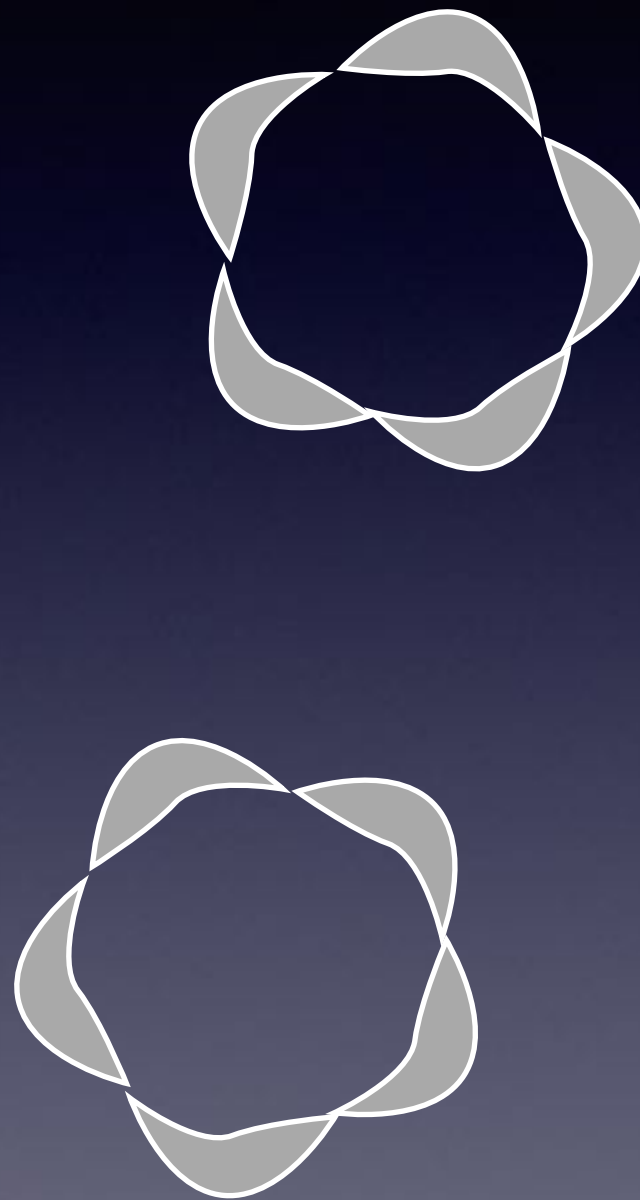


Quiescence

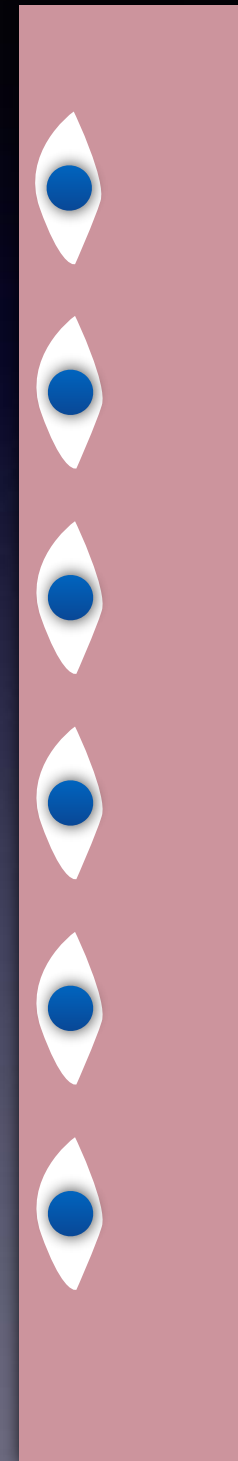
Bone



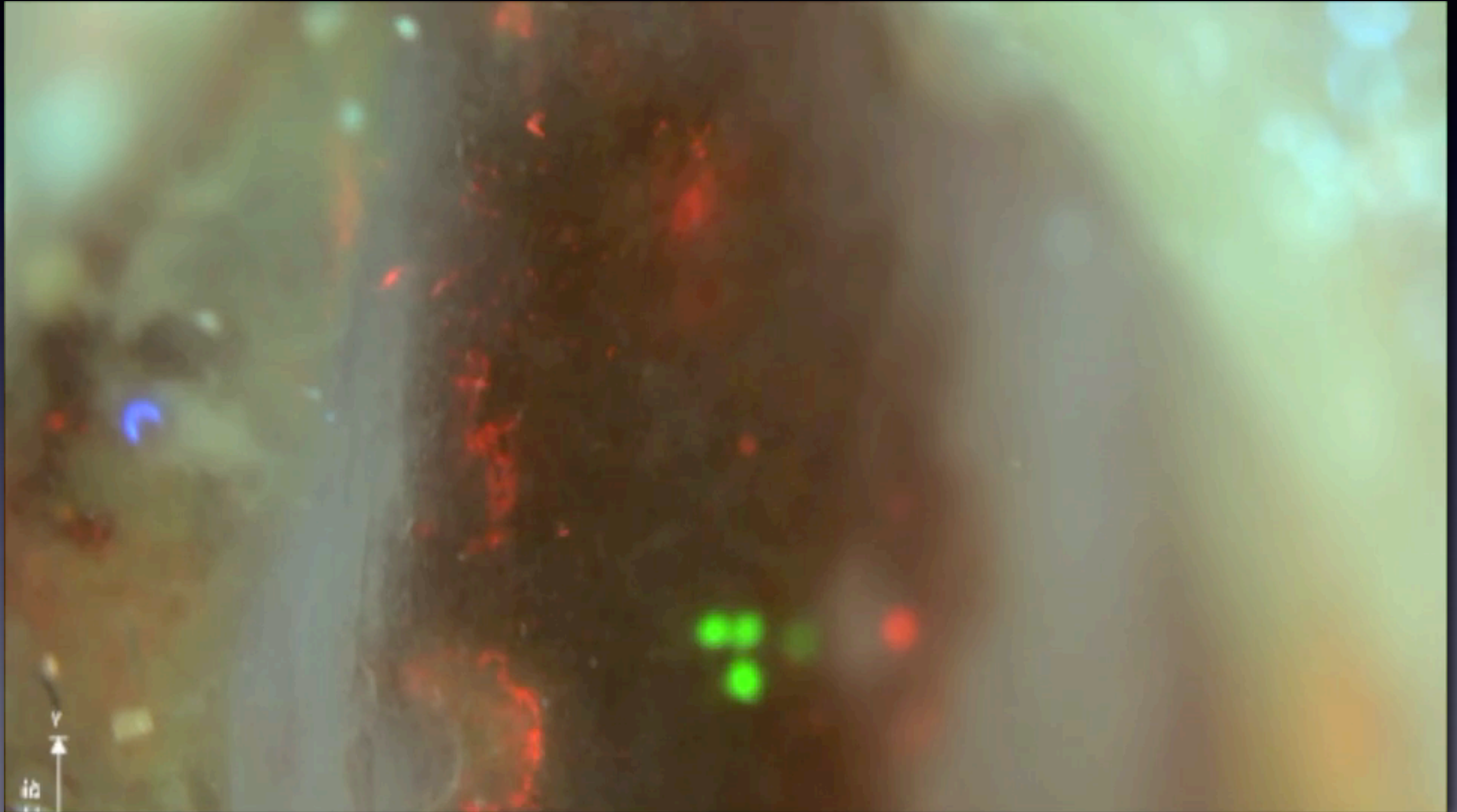
Blood Vessels



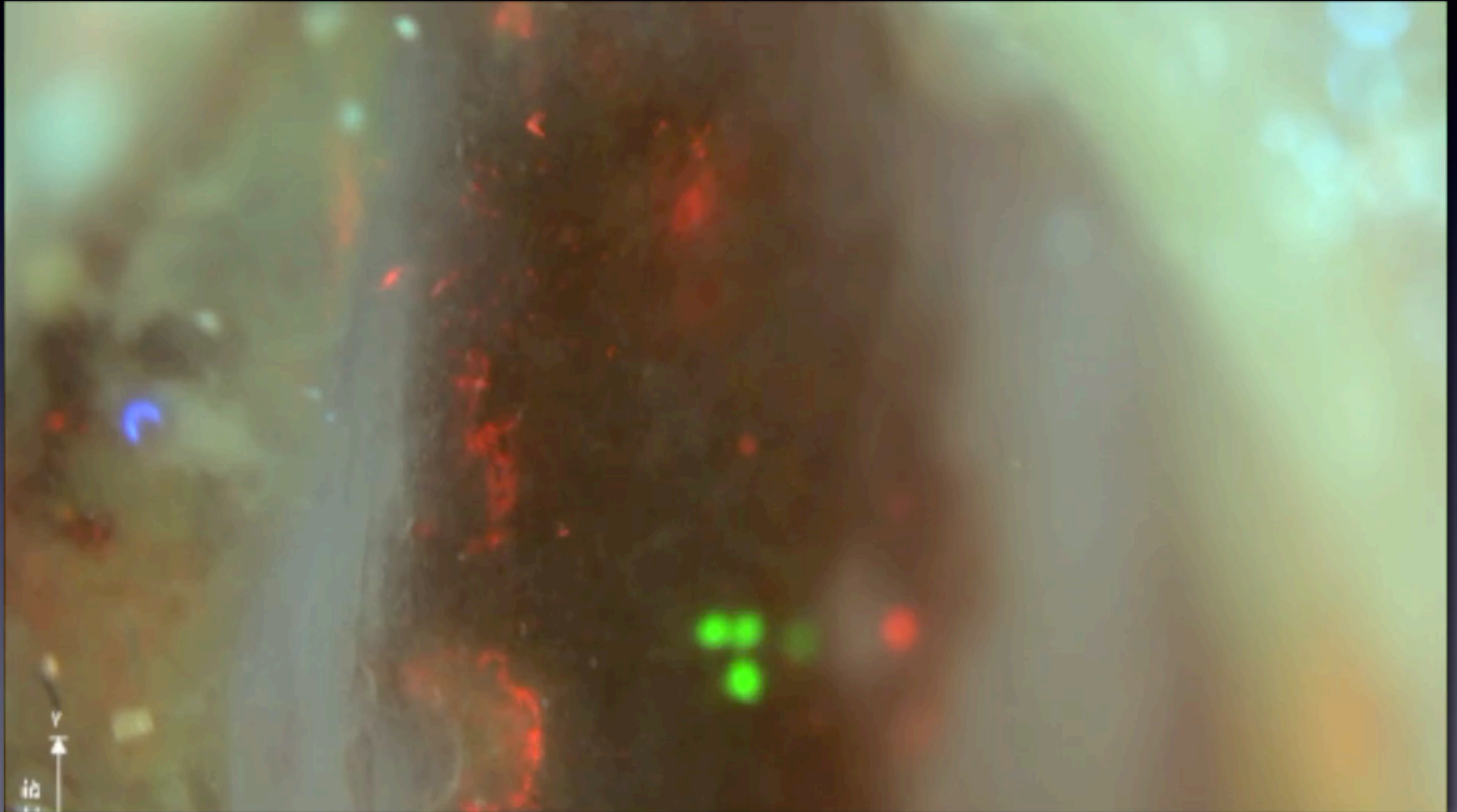
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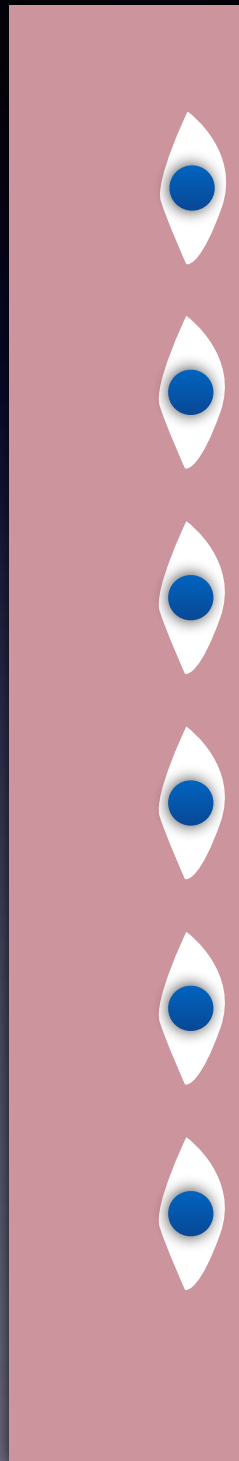
Bone Marrow Stem Cells



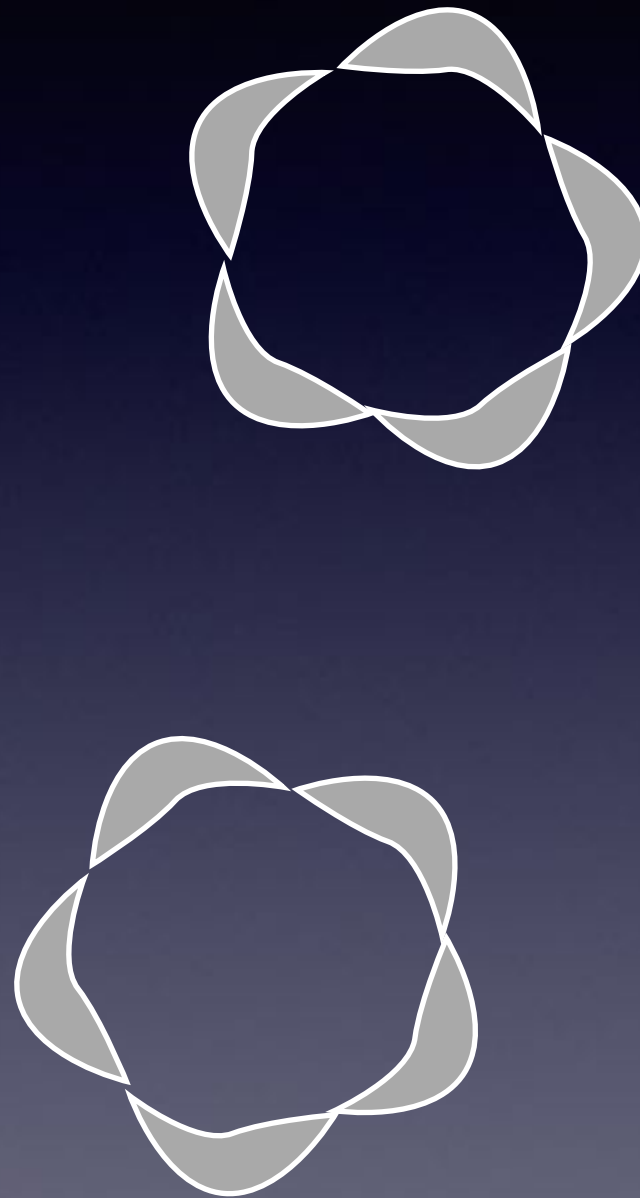
Bone Marrow Stem Cells



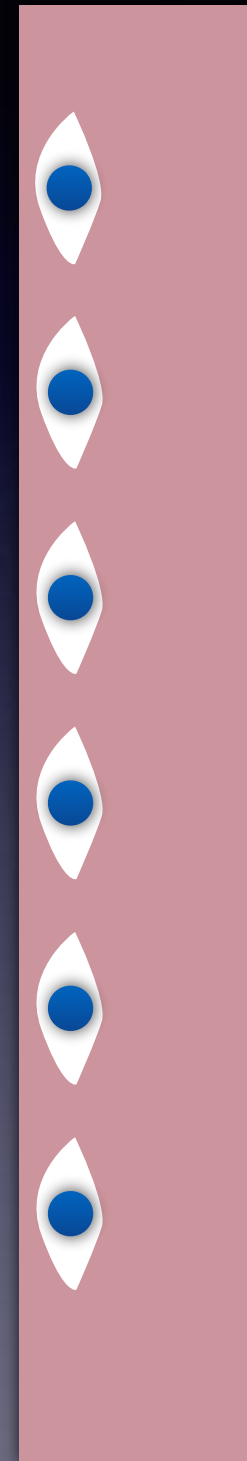
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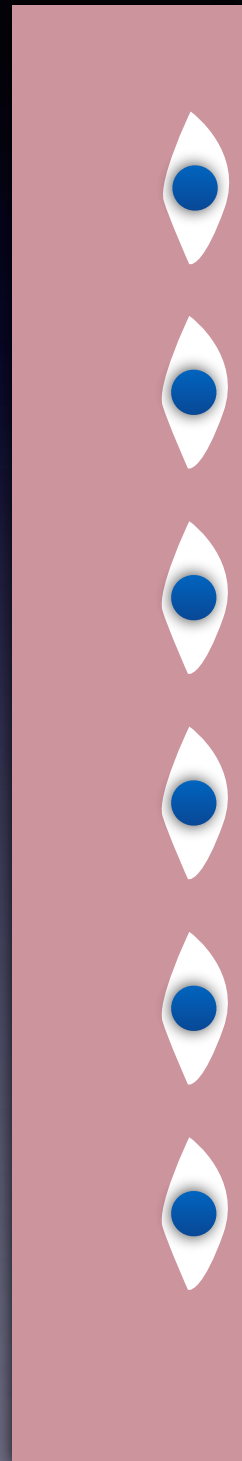
Blood Vessels



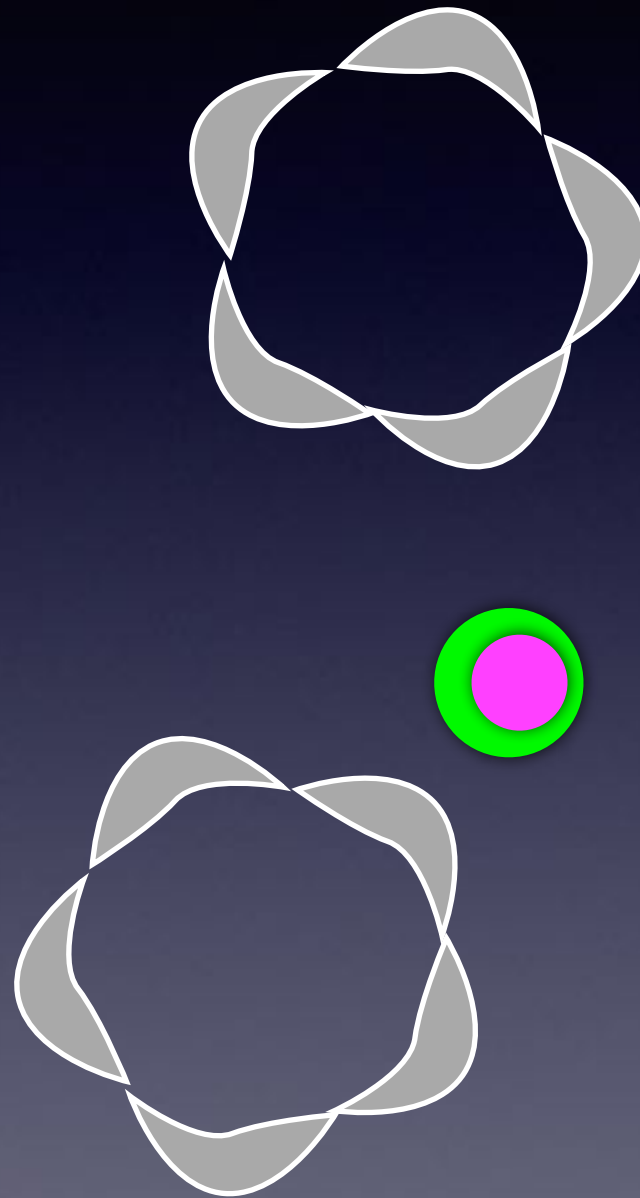
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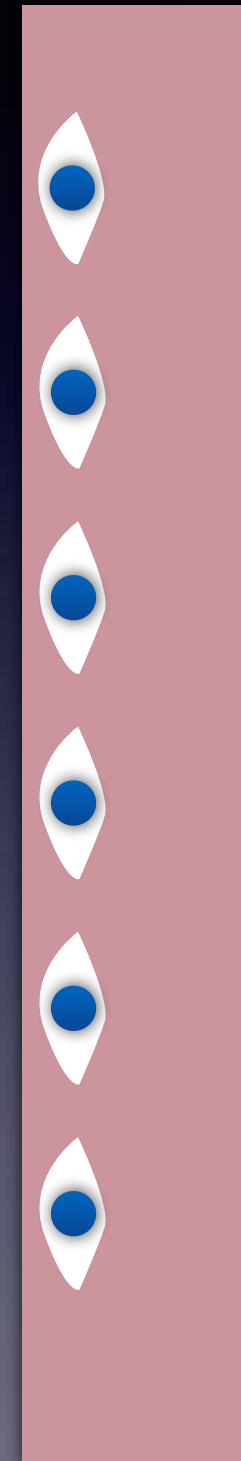
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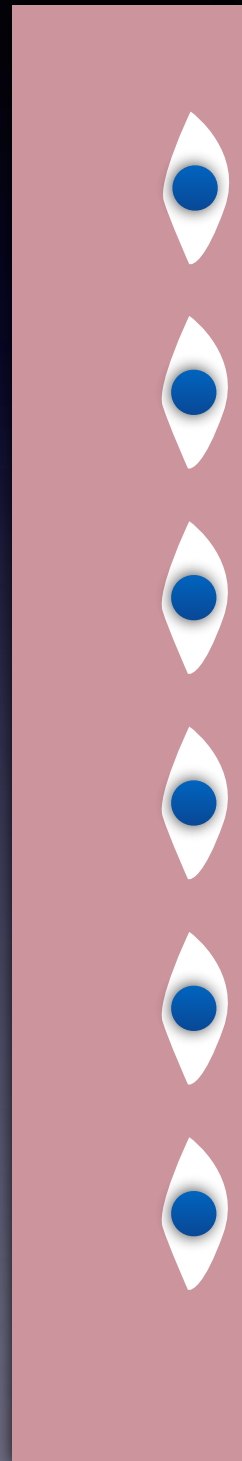
Blood Vessels



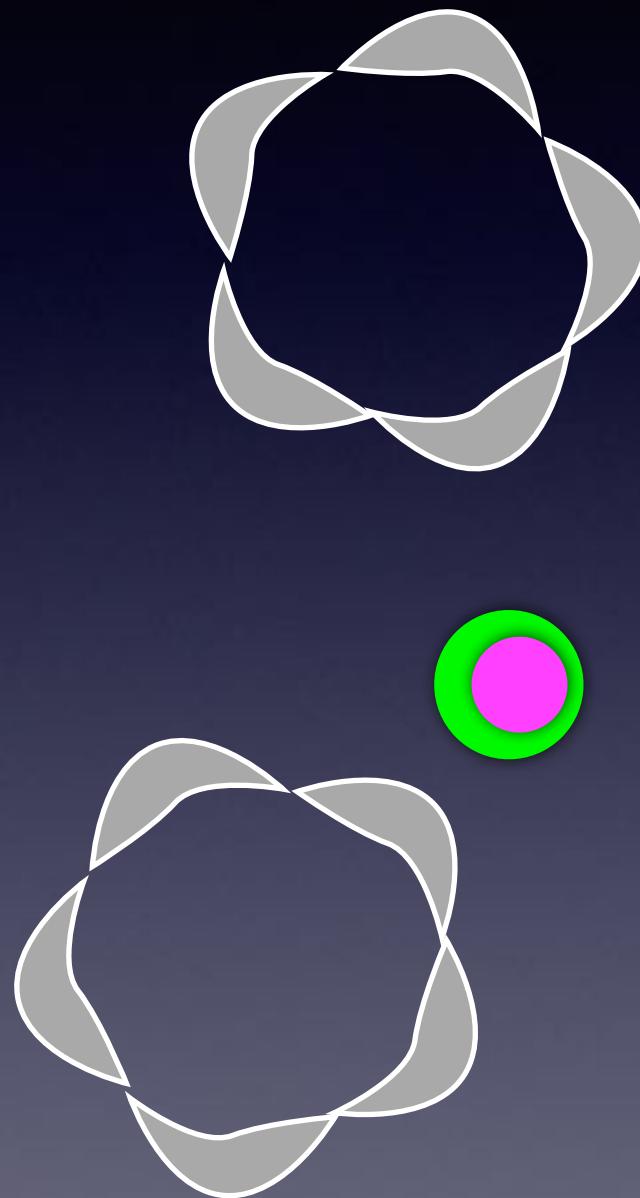
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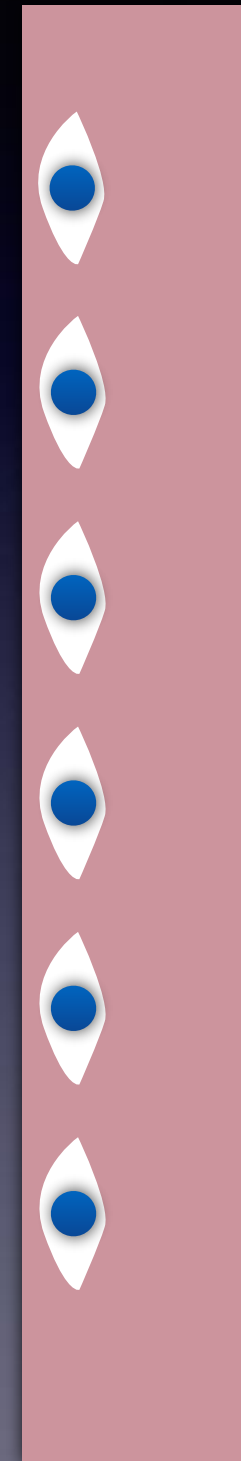
Bone



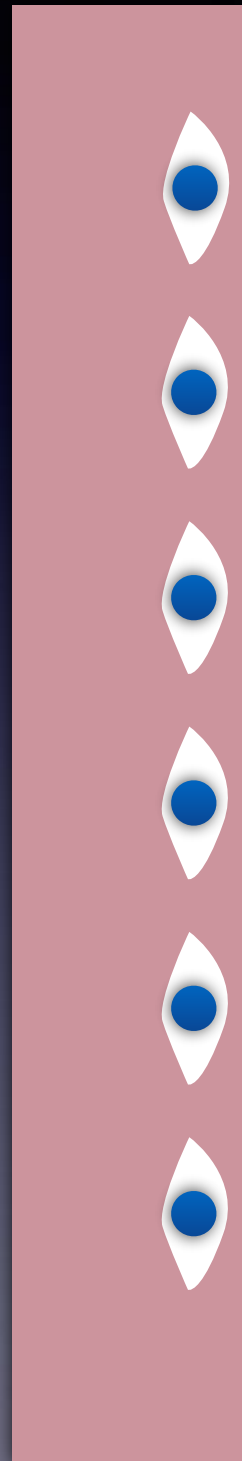
Blood Vessels



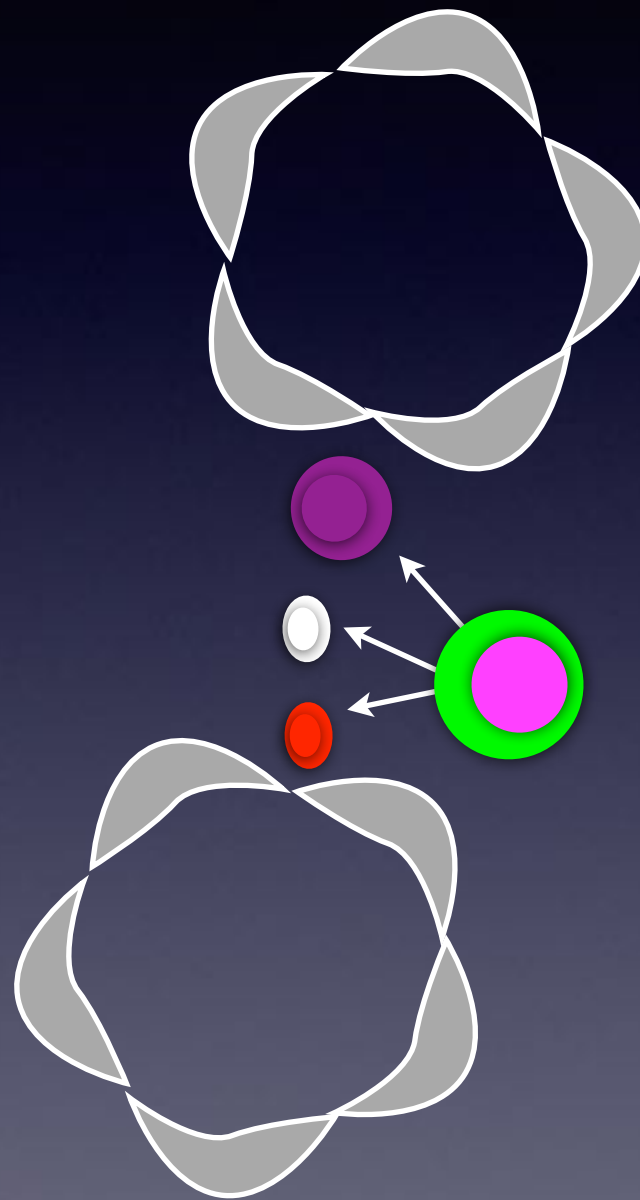
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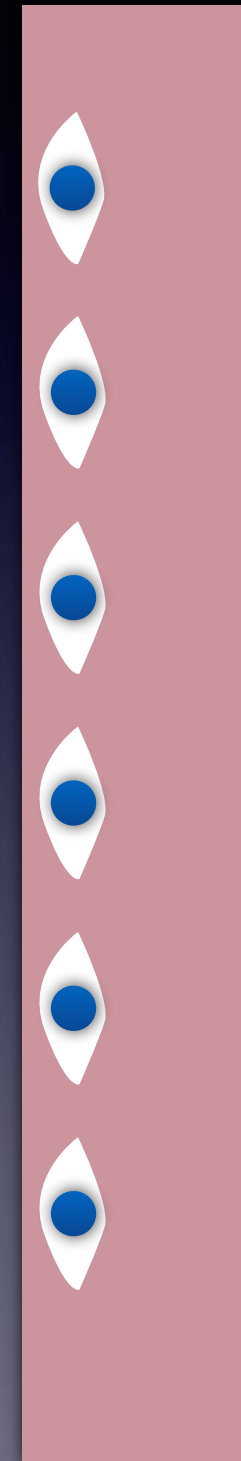
Bone



Blood Vessels



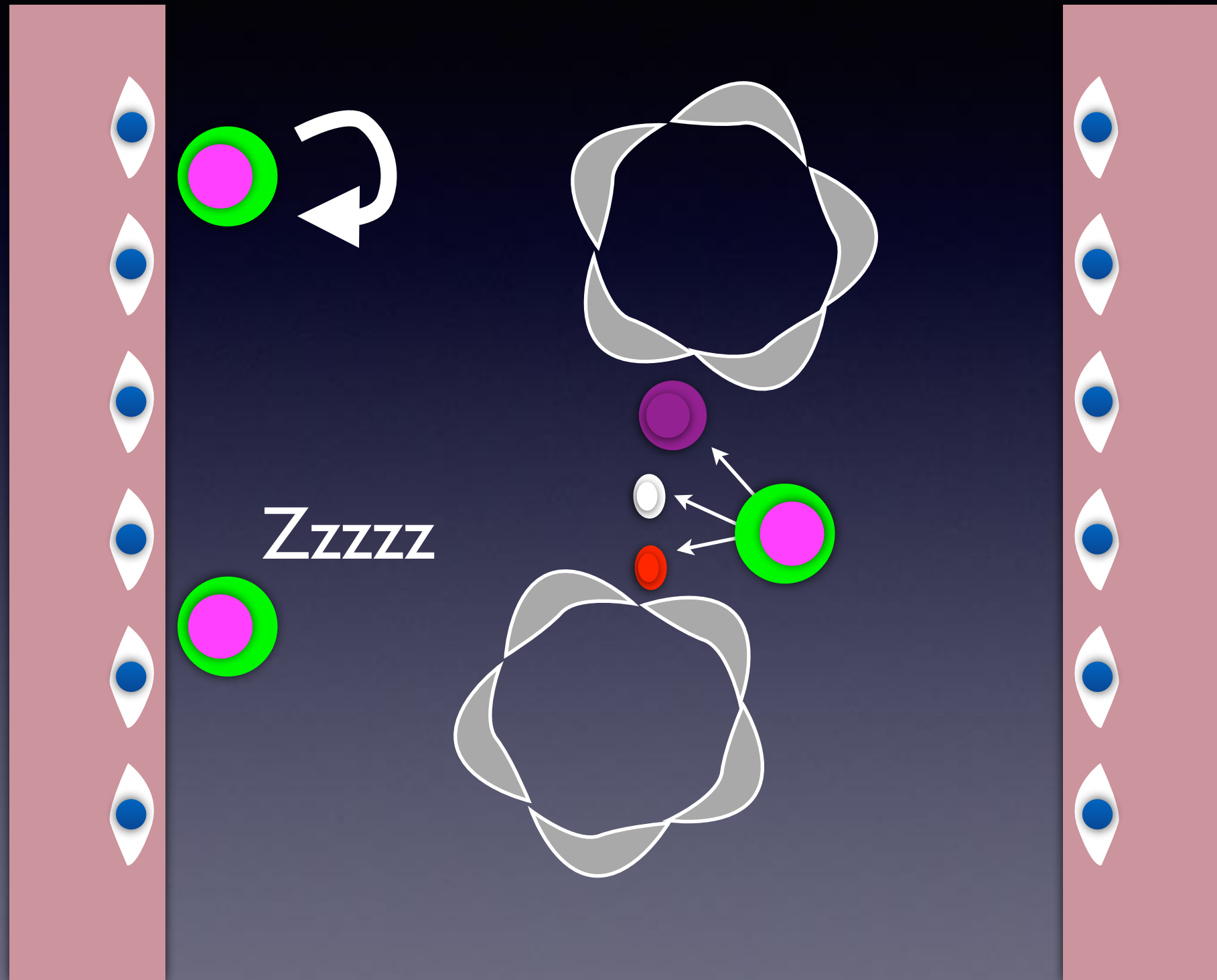
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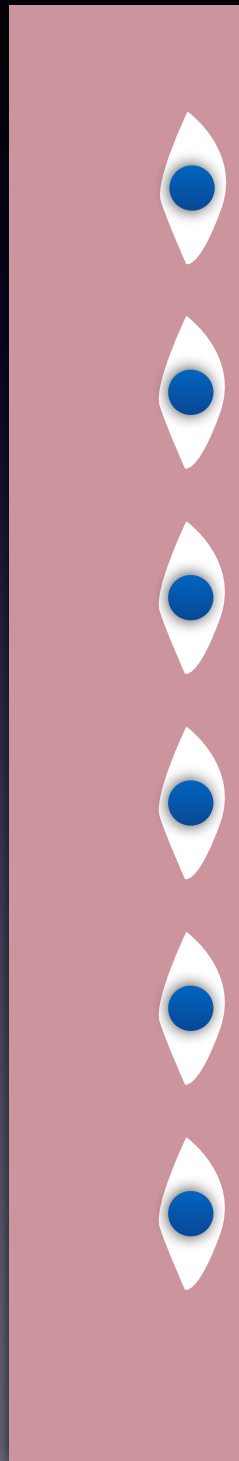
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Blood Vessels

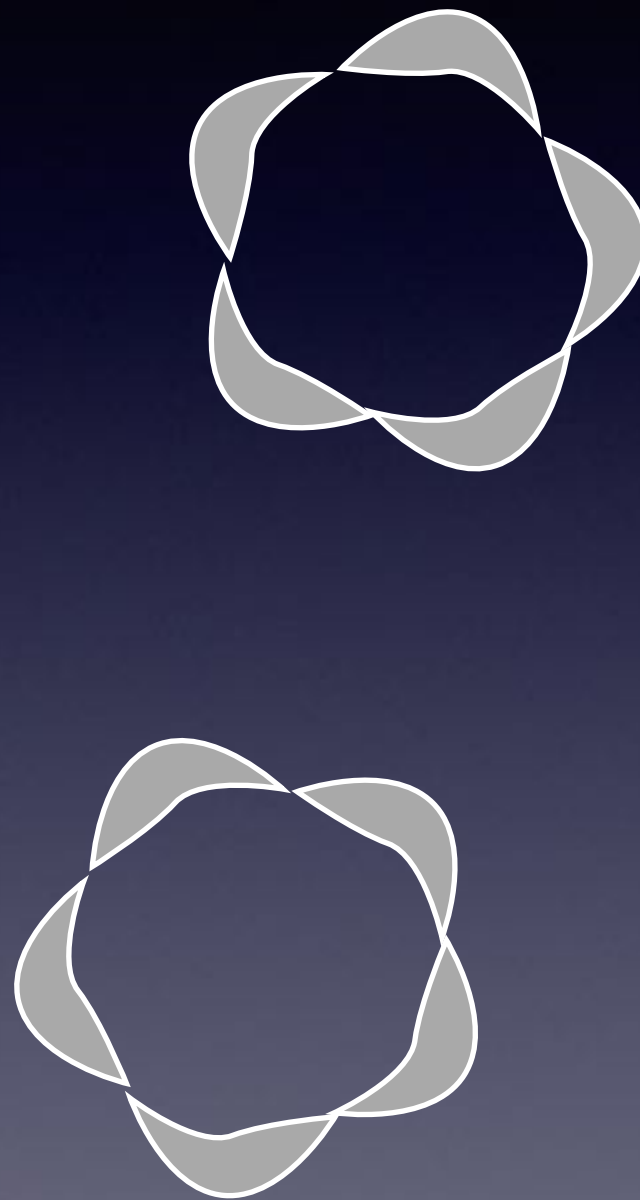
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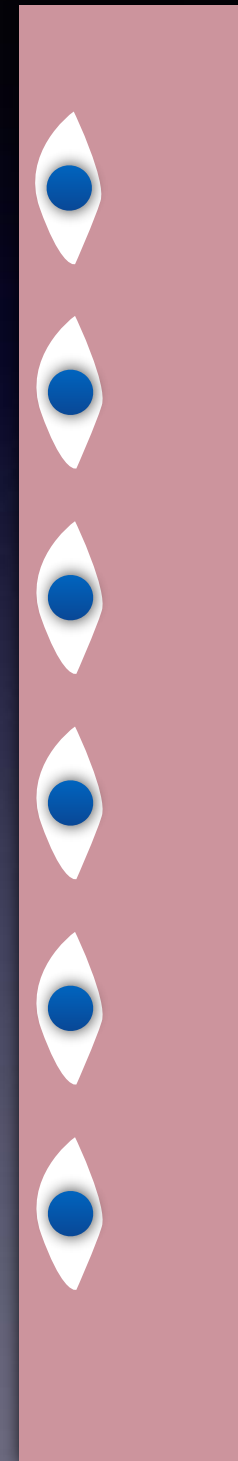
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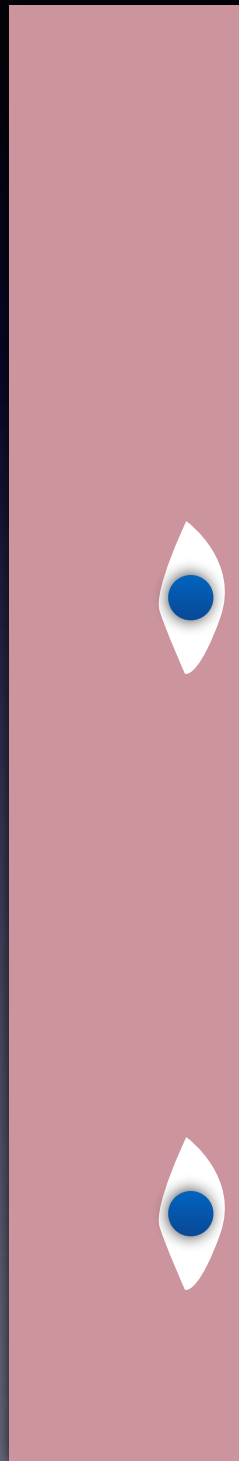
Blood Vessels



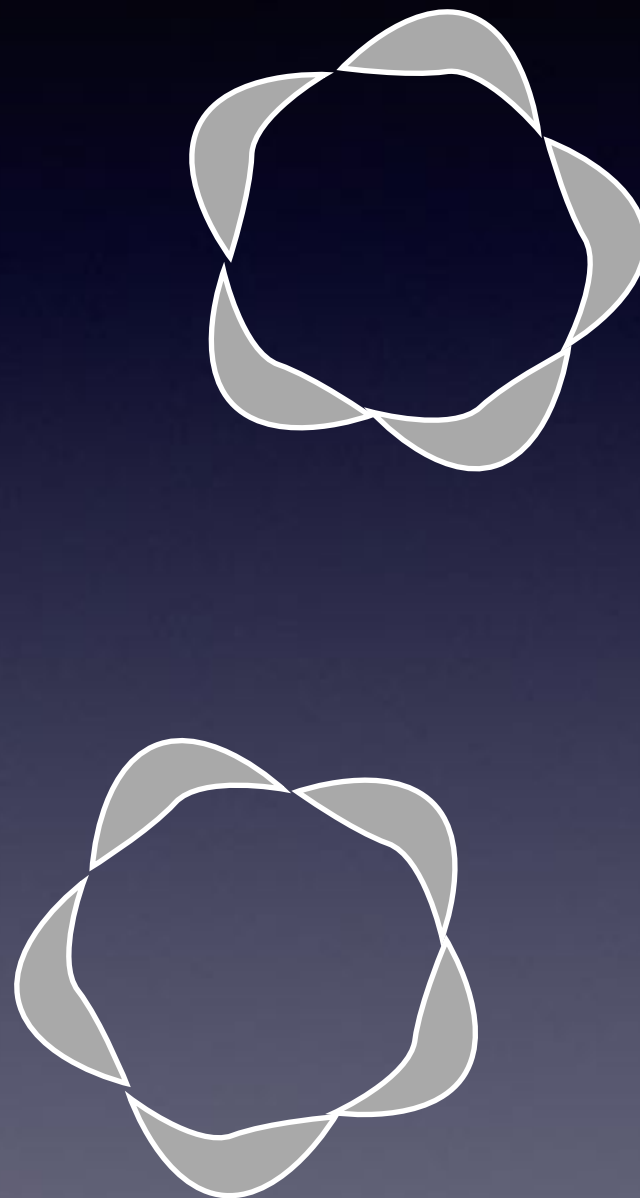
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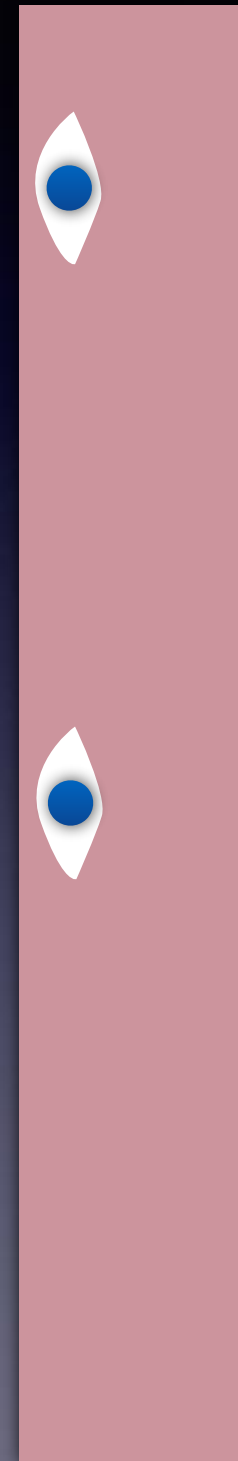
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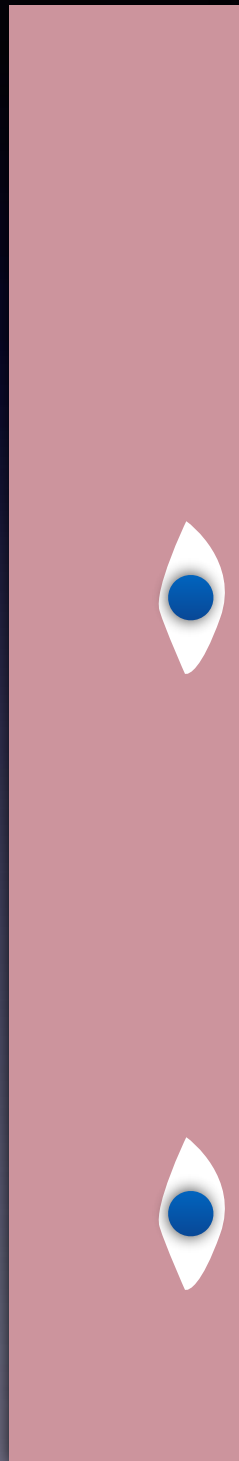
Blood Vessels



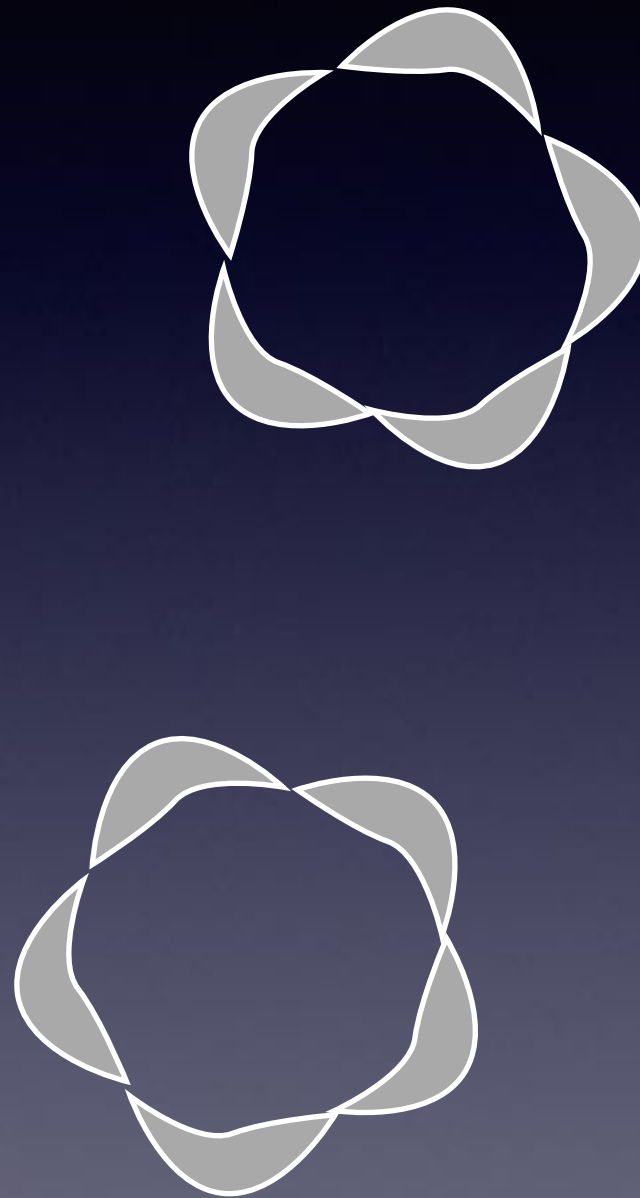
Bone



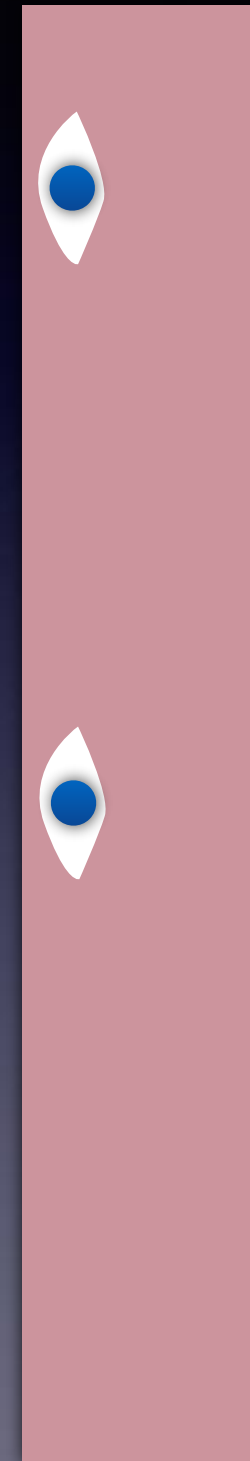
Bone



Blood Vessels



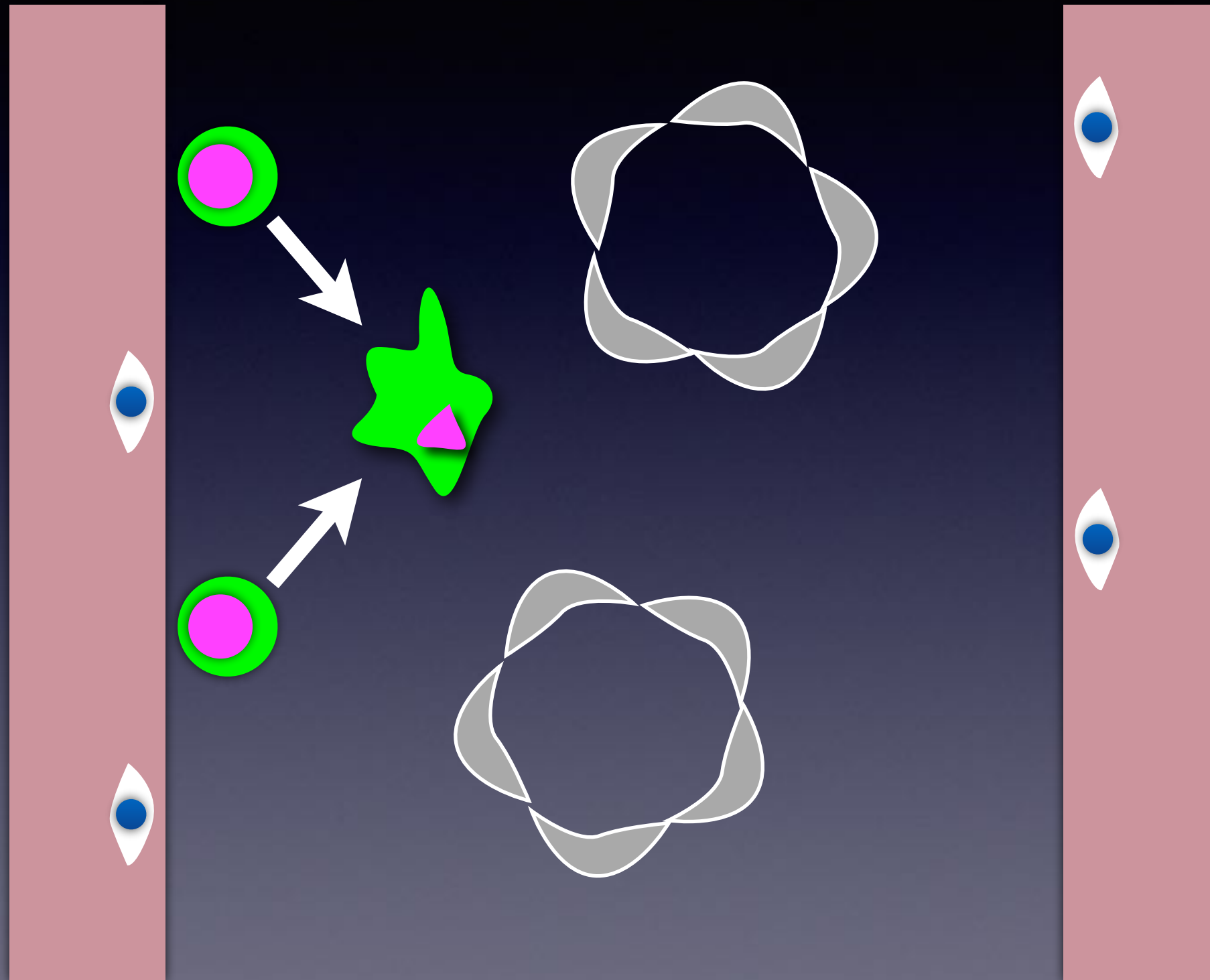
Bone



Bone

Blood Vessels

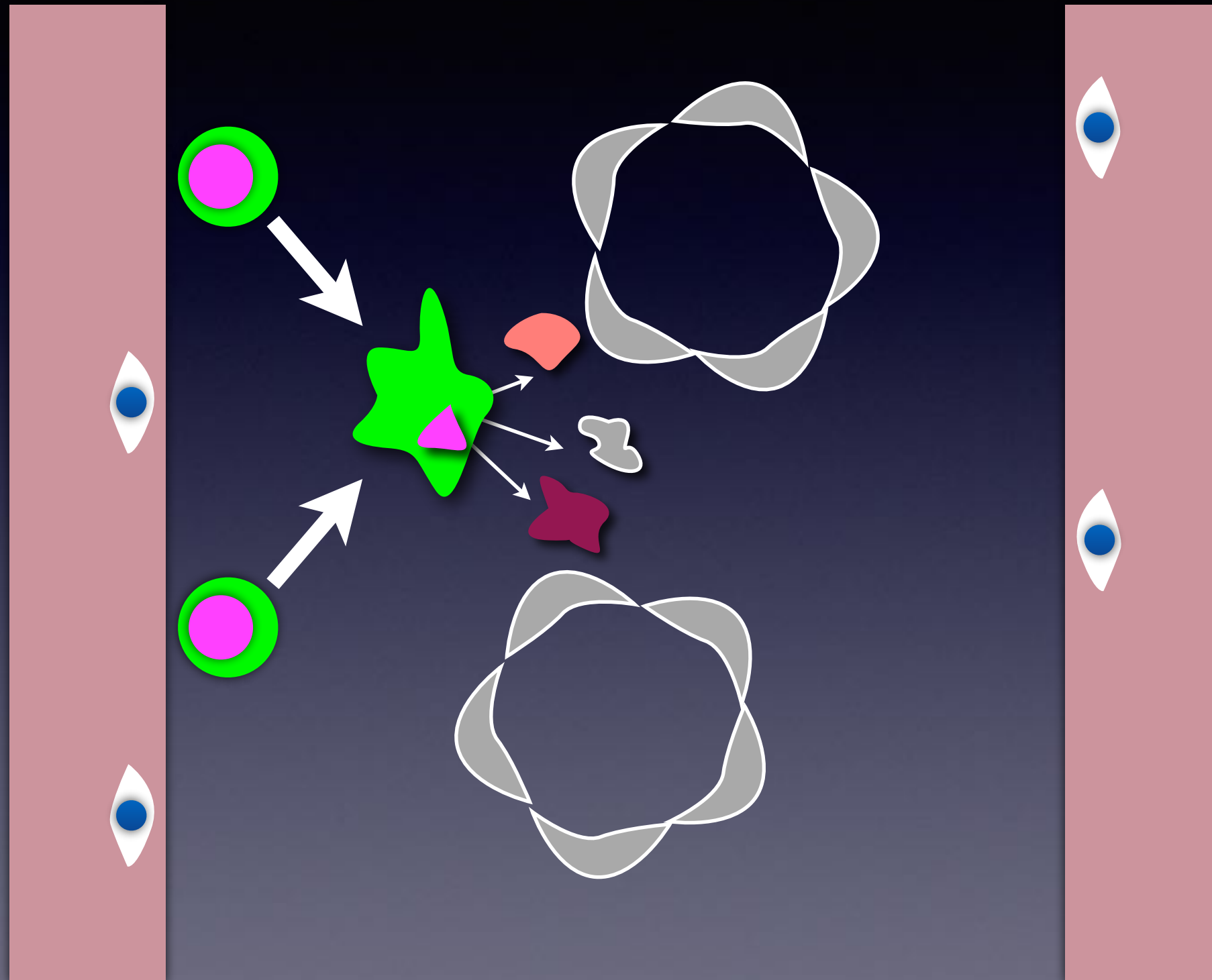
Bone



Bone

Blood Vessels

Bone



Thank you

1. Picasso Premise
2. Software Bugs
3. Clone Wars
4. Quiet Beginnings
5. Absentee Parenting

