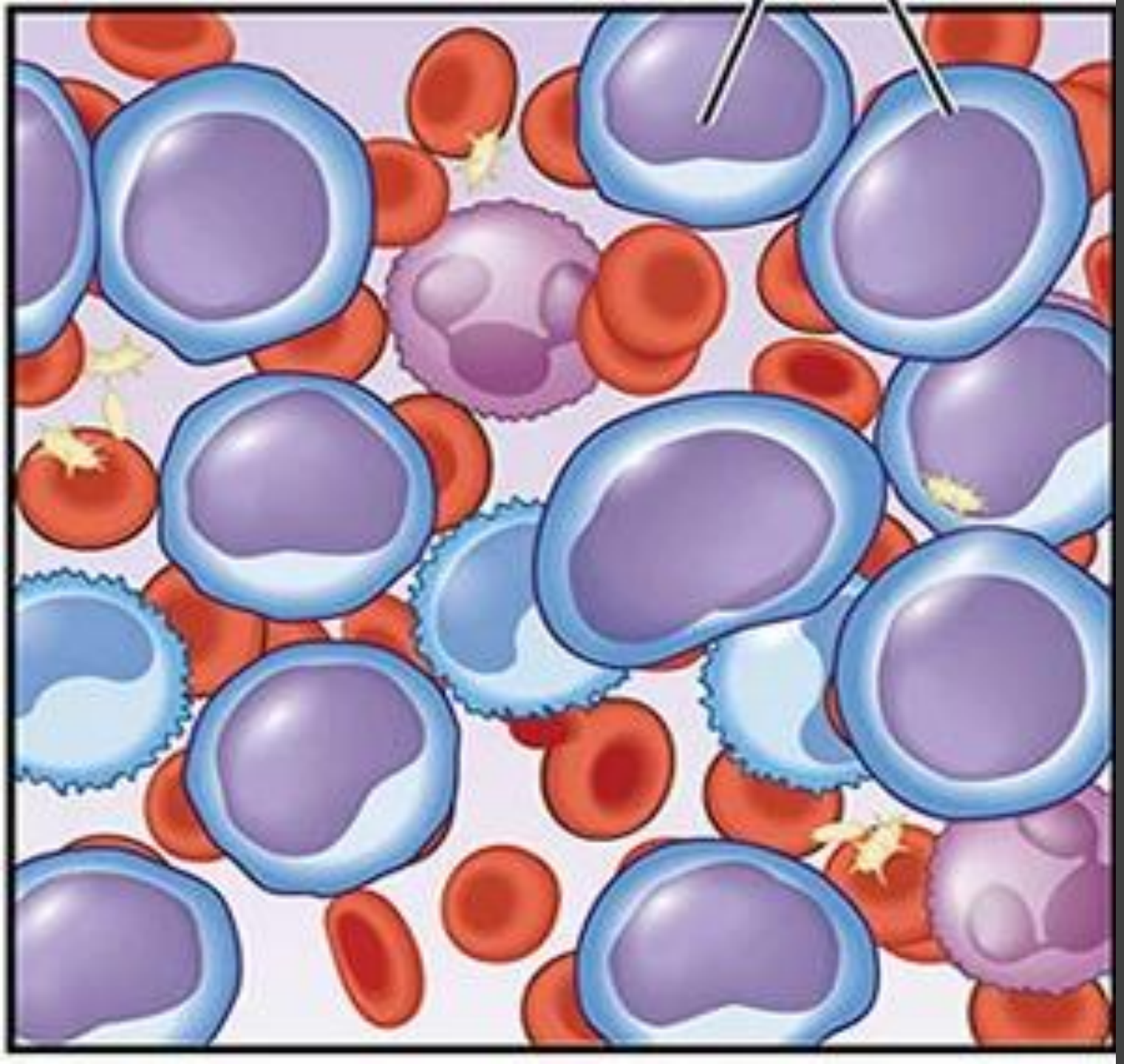


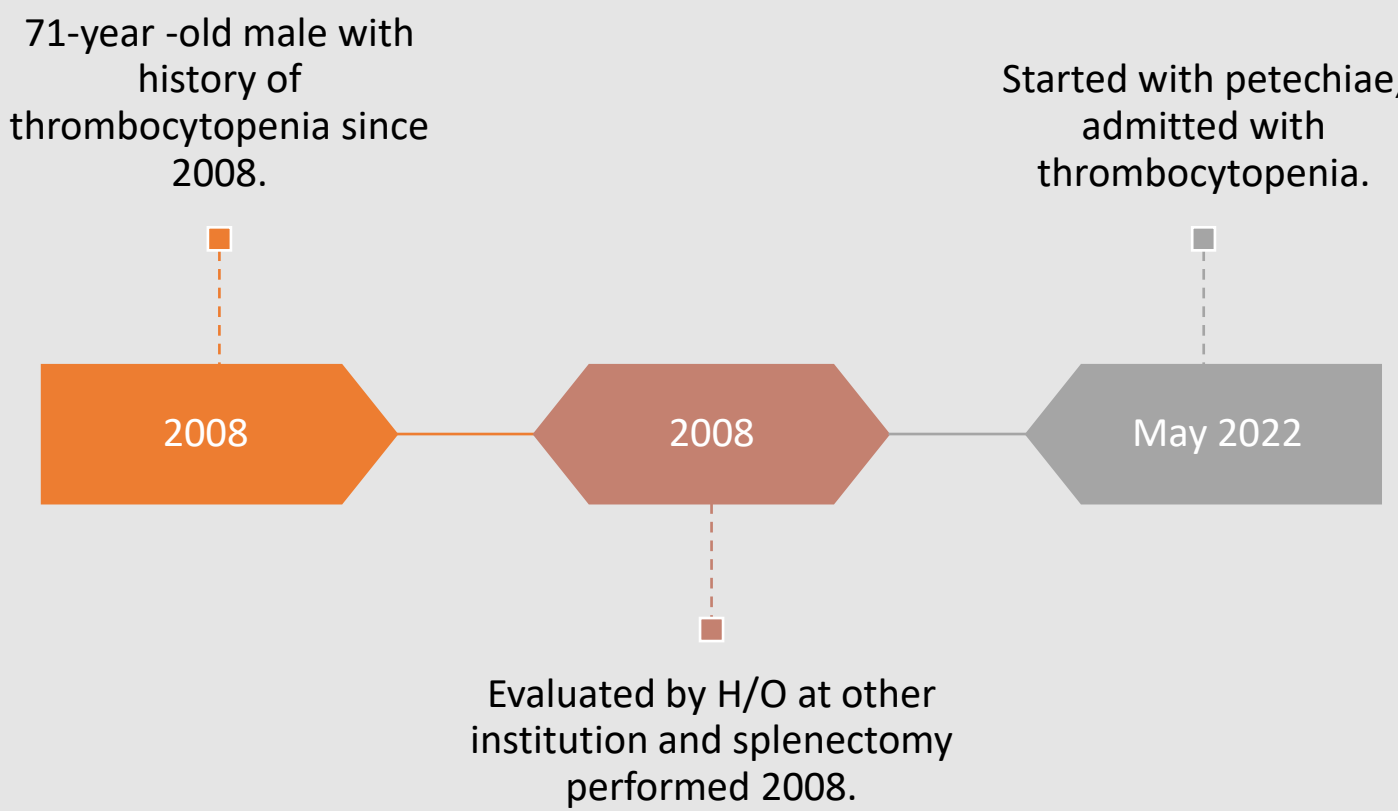
LEUKEMIA RUNX-IN BLOOD

WILLIAM D. MARRERO, MD

SAN JUAN CITY HOSPITAL-VA CARIBBEAN HEALTH CARE SYSTEM

FELLOW HEMATOLOGY-ONCOLOGY

History of Present Illness



Past Medical History

- Thrombocytopenia since 2008
- Splenectomy 2008
- HTN
- No Hx of STDs
- No toxic Habits

Family history

Father died of blood disorder

2 Sisters with diagnosis of leukemia

2 Nieces with leukemia

Physical Examination

- General
  - Well nourished, Alert and Active
  - No acute distress
- Neck
  - Supple, No JVD, No goiter.
  - No lymphadenopathy
- Lymph Nodes
  - None palpable

- Abdomen
  - Surgical Scar splenectomy
  - No palpable masses
- Skin
  - Petechias and bruises
- Neurologic
  - No gross motor or sensory deficit.

Laboratory

- **Complete blood count:**
  - **WBC: 75 x10^{-3}/mm^3**
  - **25% Blasts**
  - Hgb: 8.2g/dL
  - Plt: 48 x10-3/mm3

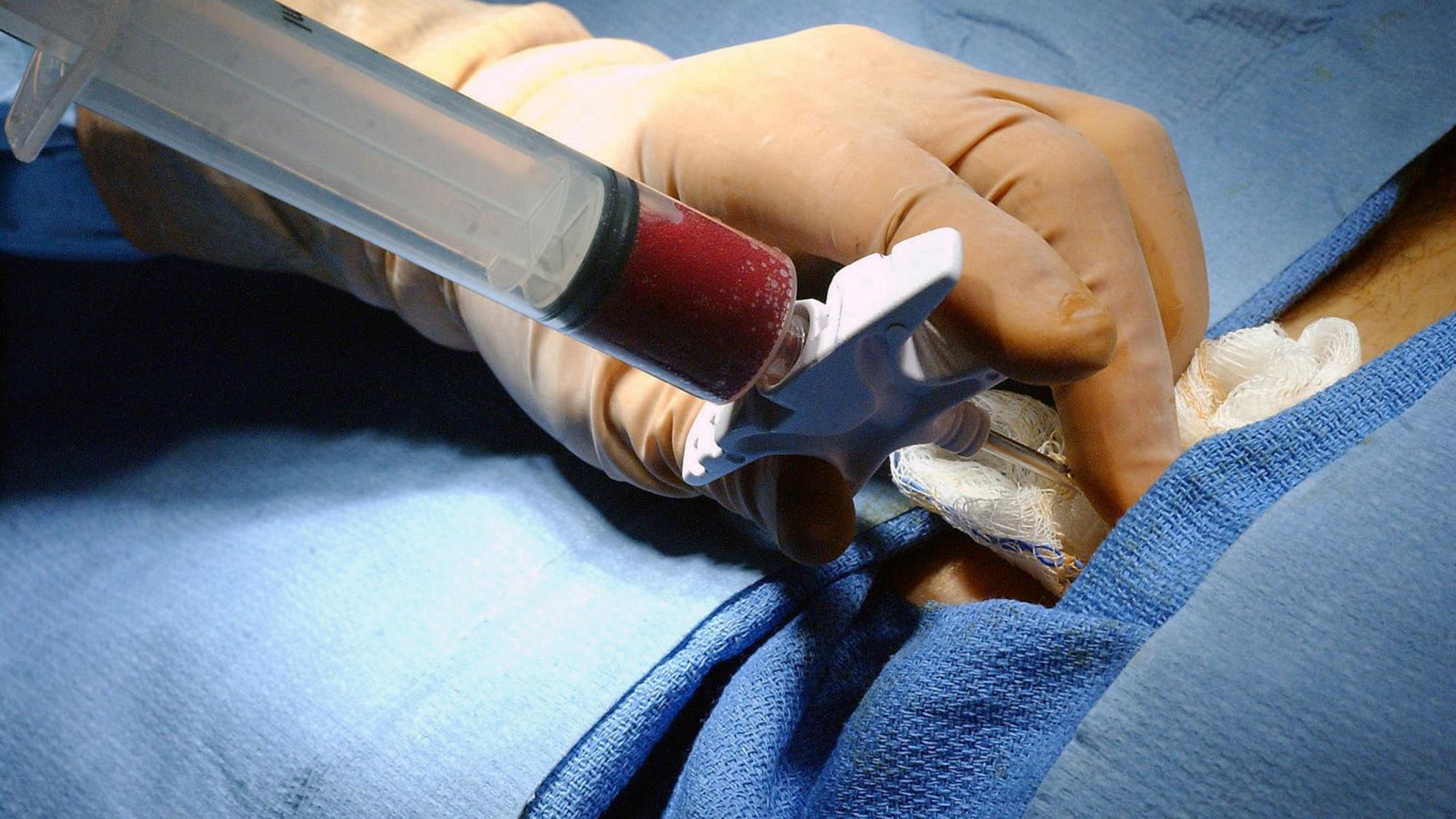
PT, PTT, Fibrinogen: WNL

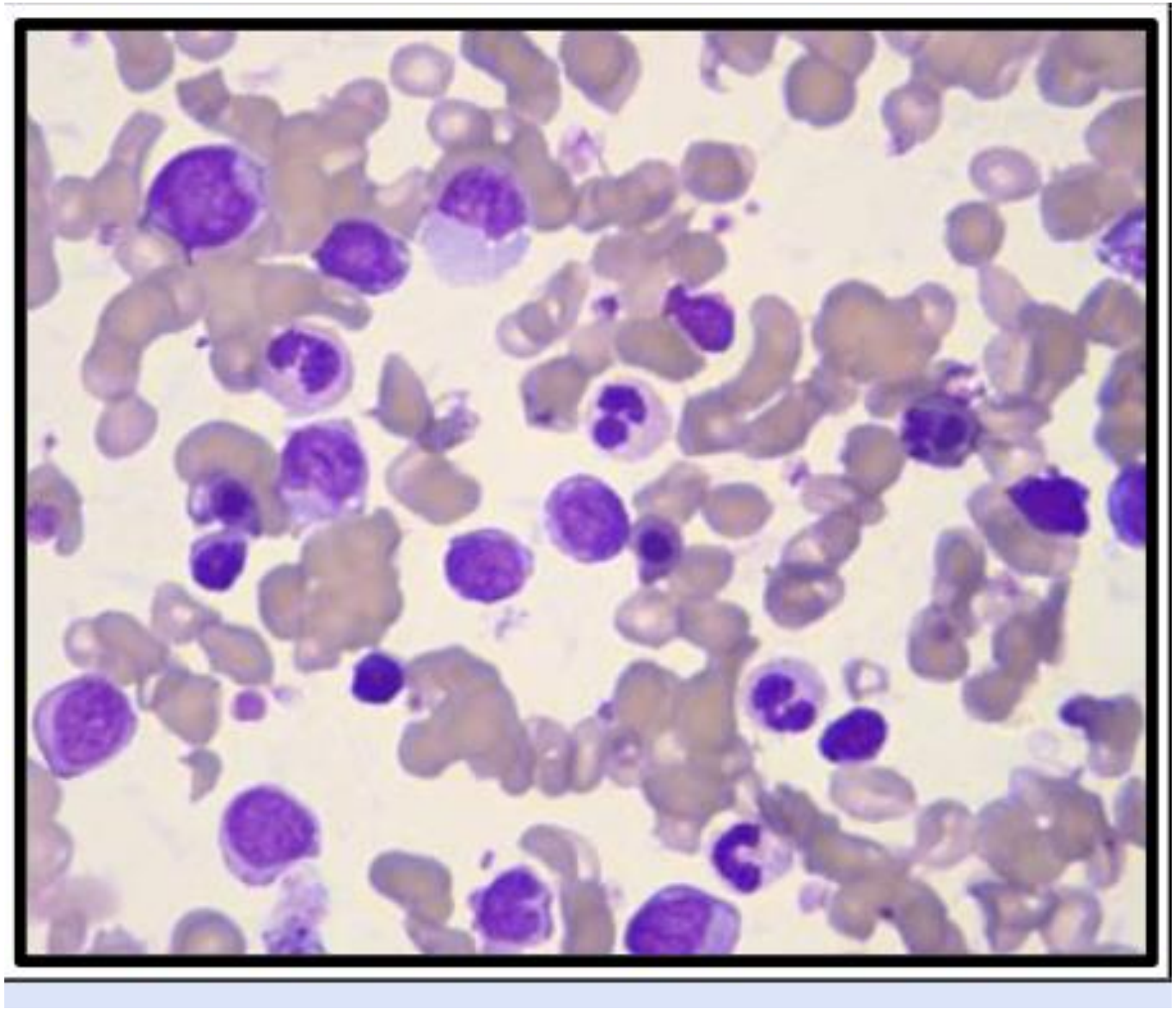
- **Blood Chemistry:**
  - ✓ **WNL**

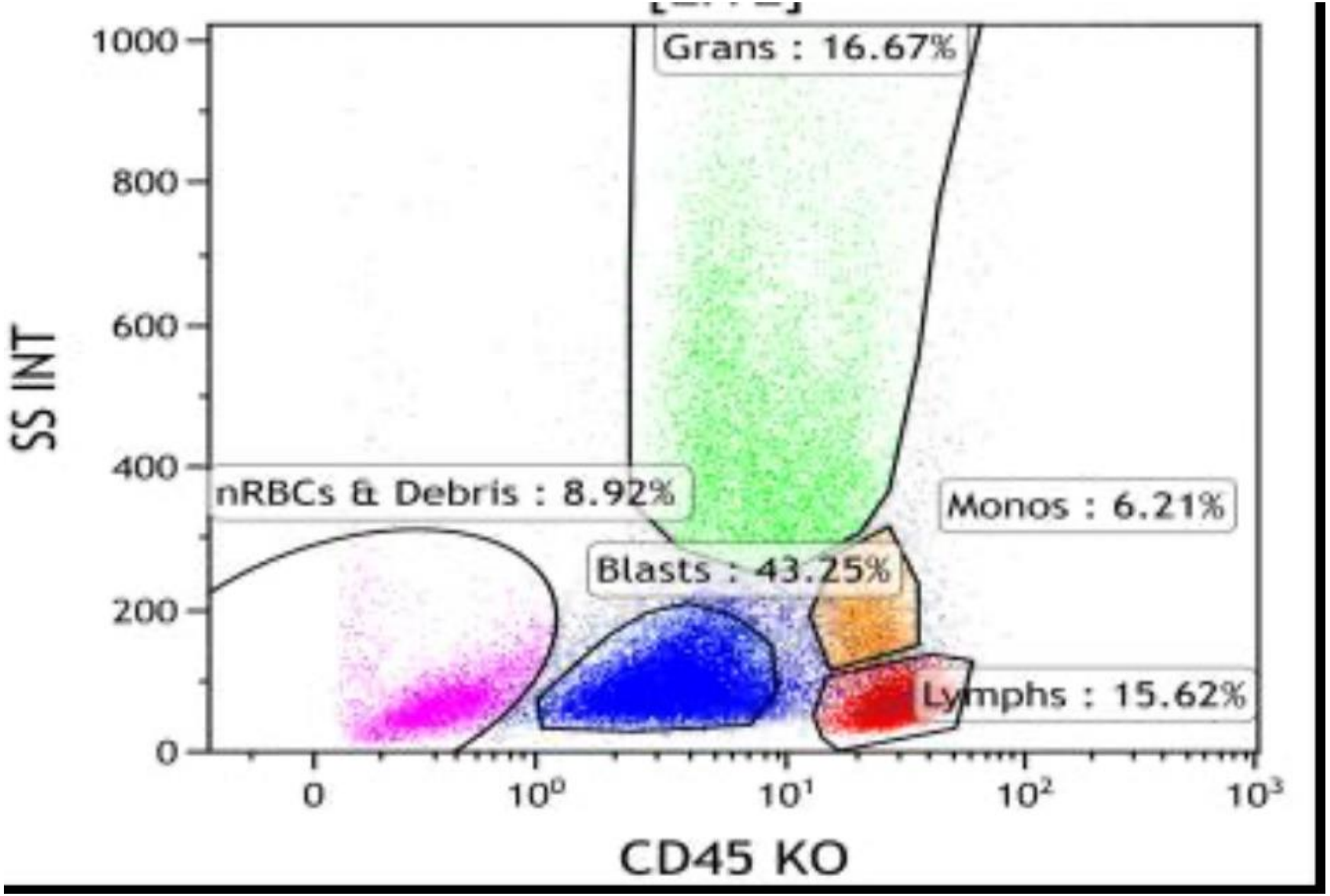
Other Labs:

HIV: non detected

Hepatitis panel: non detected

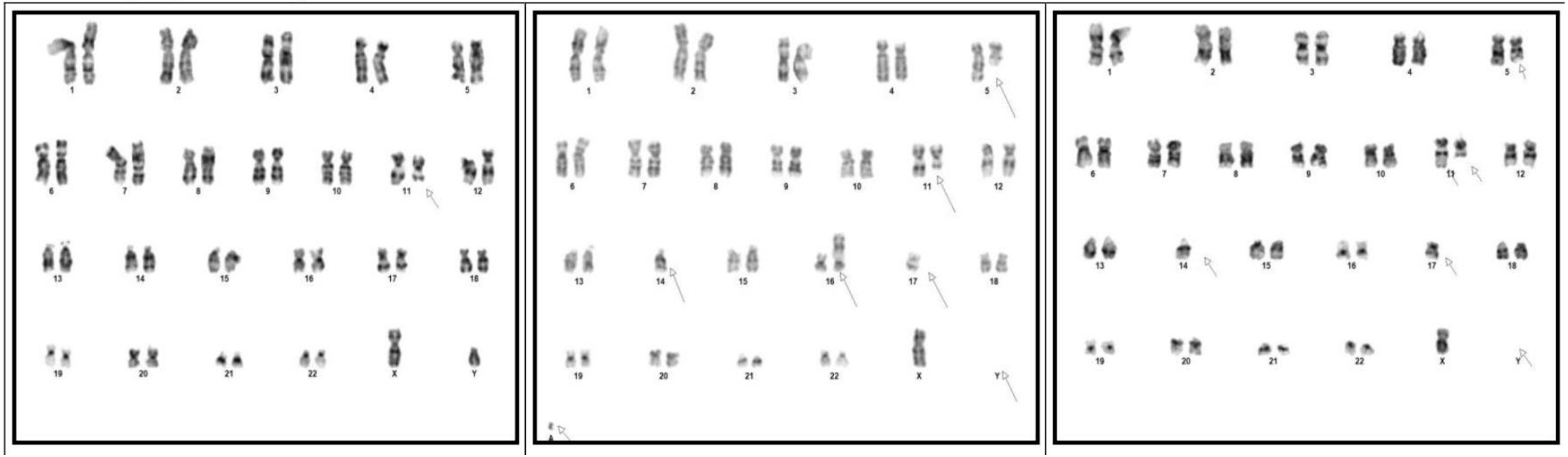





Grans : 16.67%
nRBCs & Debris : 8.92%
Monos : 6.21%
Blasts : 43.25%
Lymphs : 15.62%
SS INT
CD45 KO
1000
800
600
400
200
0
0
10⁰
10¹
10²
10³

Cytogenetic Karyotype

submicroscopic genetic changes.



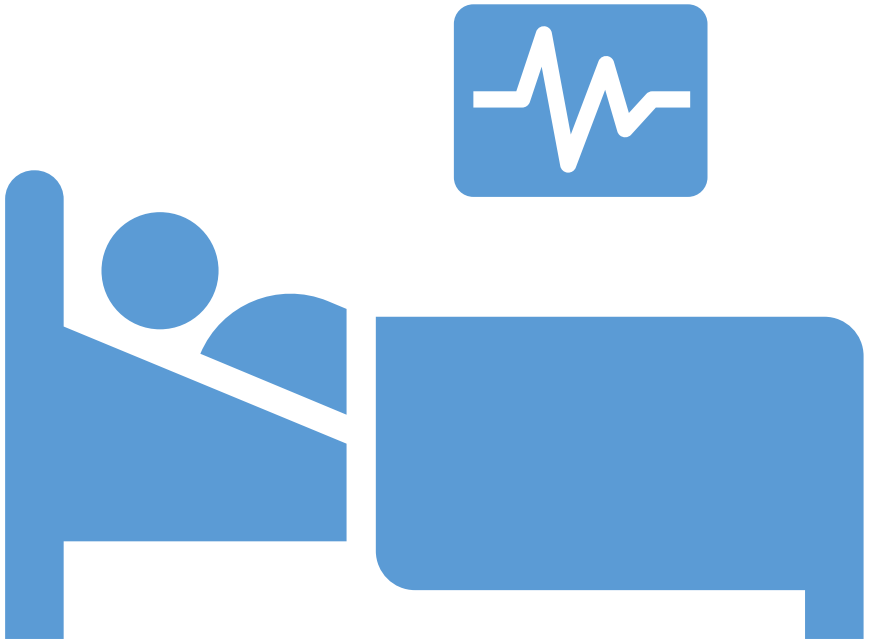
46,XY,add(11)(q14)[7]/43-44,idem,-Y,add(5)(q11.2),der(5;14)(p10;q10),add(11)(q23),-14,der(16)t(14;16)(q11.2;p13.1),del(16)(p13.1),-17,+mar,inc[cp13];

Abnormal Male Karyotype

Molecular Markers

RUNX-1: VAF 53%

Case Analysis



- Patient with AML; RUNX1 VAF > 50%
  - Family history of leukemia
    - RUNX1; Germline predisposition?

Extended Hereditary Cancer Test

Gene	Variant	Zygosity	Classification
RUNX1	c.611 G>A p.(R204Q)	Heterozygous	Pathogenic Variant

Table 3. Clinical features prompting consideration of clinical testing for a germline predisposition allele(s)

Clinical features
Personal history of ≥2 cancers, one of which is a hematopoietic malignancy (order does not matter)
Personal history of a hematopoietic malignancy plus: • Another relative within two generations with another hematopoietic malignancy, or • Another relative within two generations with a solid tumor diagnosed at age 50 or younger, or • Another relative within two generations with other hematopoietic abnormalities

Germline Predisposition

SPECIAL REPORT | SEPTEMBER 22, 2022

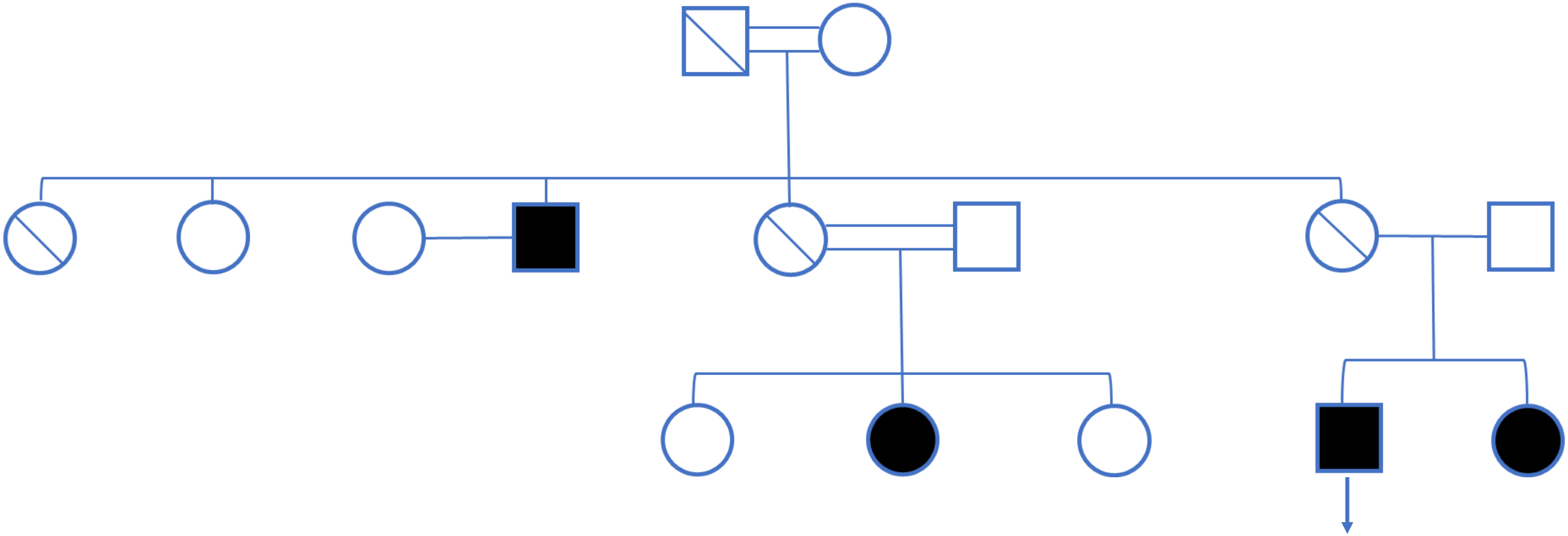
Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN

Hartmut Döhner, Andrew H. Wei, Frederick R. Appelbaum, Charles Craddock, Courtney D. DiNardo, Hervé Dombret, Benjamin L. Ebert, Pierre Fenaux, Lucy A. Godley, Robert P. Hasserjian, Richard A. Larson, Ross L. Levine, Yasushi Miyazaki, Dietger Niederwieser, Gert Ossenkoppele, Christoph Röllig, Jorge Sierra, Eytan M. Stein, Martin S. Tallman, Hwei-Fang Tien, Jianxiang Wang, Agnieszka Wierzbowska, Bob Löwenberg

Blood (2022) 140 (12): 1345–1377.

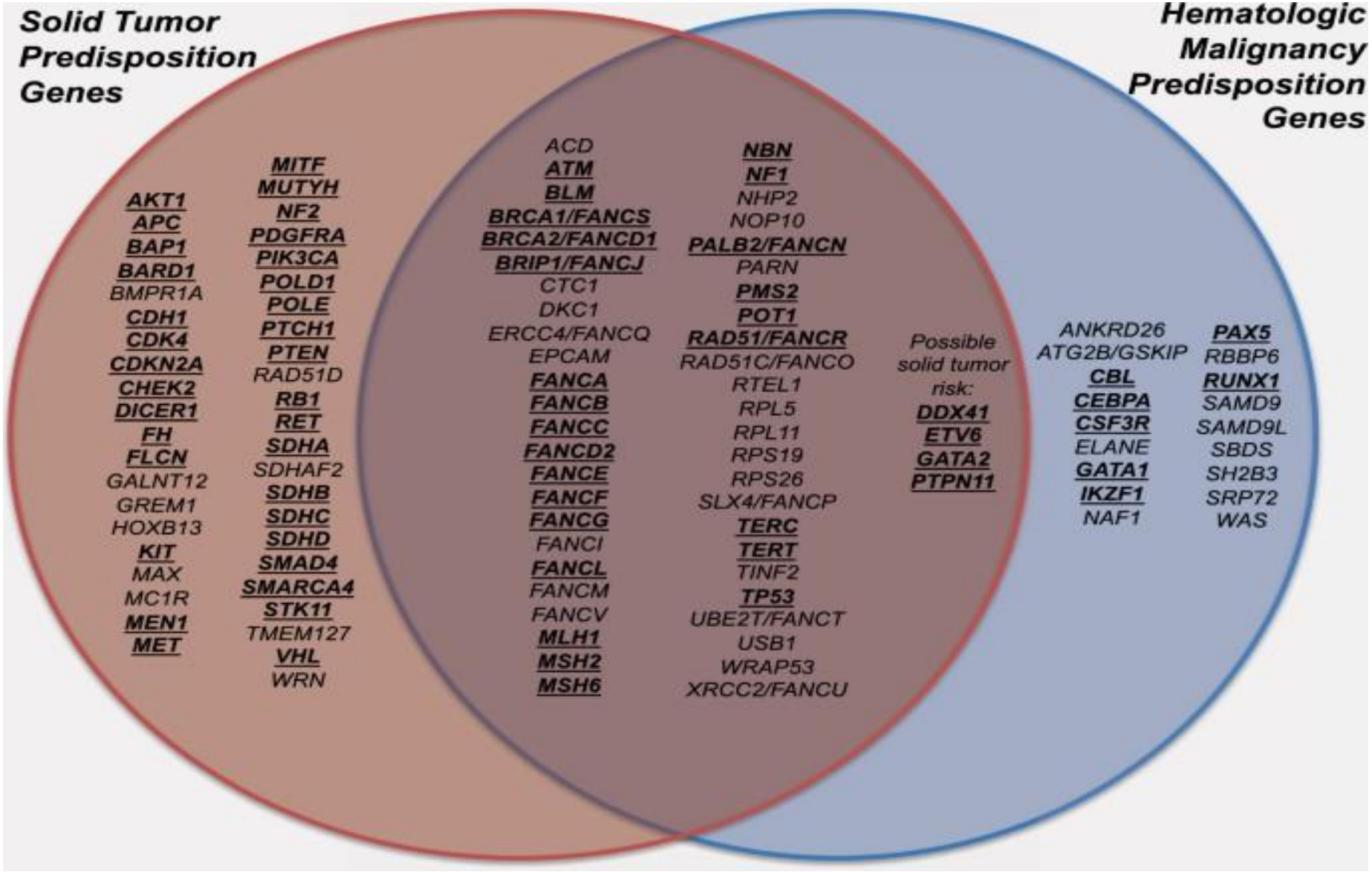
A variant is deemed germline if:

- it is detected in DNA derived from a tissue source not likely to undergo somatic mutation frequently and at a variant allele frequency consistent with the germline (generally 30–60%); or
- it is identified in ≥2 relatives at a variant allele frequency consistent with the germline.



exon 5 of the RUNX1 gene

Pathogenic Variant.


Solid Tumor Predisposition Genes
Hematologic Malignancy Predisposition Genes
AKT1
APC
BAP1
BARD1
BMPR1A
CDH1
CDK4
CDKN2A
CHEK2
DICER1
FH
FLCN
GALNT12
GREM1
HOXB13
KIT
MAX
MC1R
MEN1
MET
MITF
MUTYH
NF2
PDGFRA
PIK3CA
POLD1
POLE
PTCH1
PTEN
RAD51D
RB1
RET
SDHA
SDHAF2
SDHB
SDHC
SDHD
SMAD4
SMARCA4
STK11
TMEM127
VHL
WRN
ACD
ATM
BLM
BRCA1/FANCS
BRCA2/FANCD1
BRIP1/FANCJ
CTC1
DKC1
ERCC4/FANCQ
EPCAM
FANCA
FANCB
FANCC
FANCD2
FANCE
FANCF
FANCG
FANCI
FANCL
FANCM
FANCV
MLH1
MSH2
MSH6
NBN
NF1
NHP2
NOP10
PALB2/FANCN
PARN
PMS2
POT1
RAD51/FANCR
RAD51C/FANCO
RTEL1
RPL5
RPL11
RPS19
RPS26
SLX4/FANCP
TERC
TERT
TINF2
TP53
UBE2T/FANCT
USB1
WRAP53
XRCC2/FANCU
Possible solid tumor risk:
DDX41
ETV6
GATA2
PTPN11
ANKRD26
ATG2B/GSKIP
CBL
CEBPA
CSF3R
ELANE
GATA1
IKZF1
NAF1
PAX5
RBBP6
RUNX1
SAMD9
SAMD9L
SBDS
SH2B3
SRP72
WAS


Thank
LEUKEMIA
You