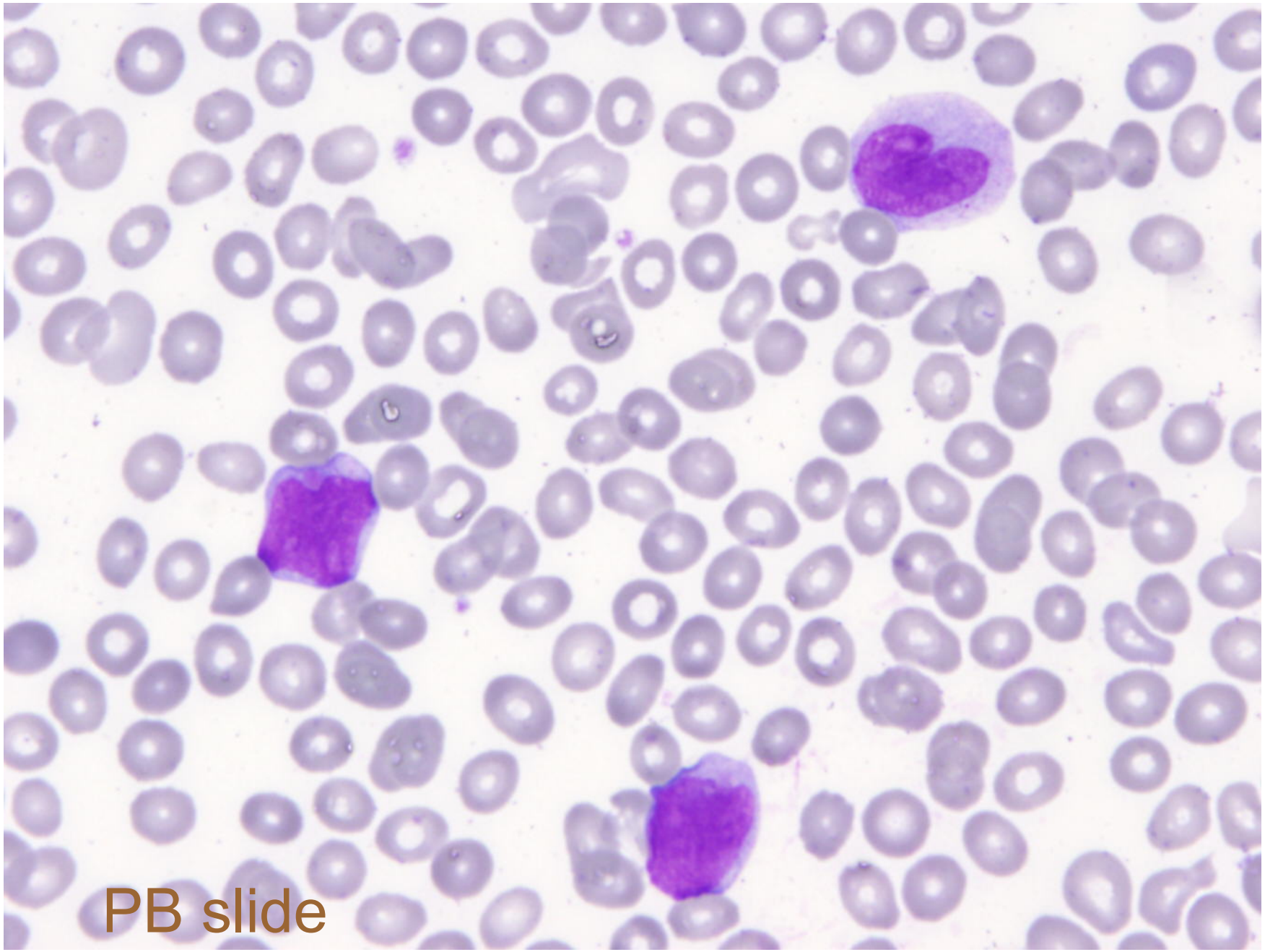
Integrated diagnosis of AML: a real-life example

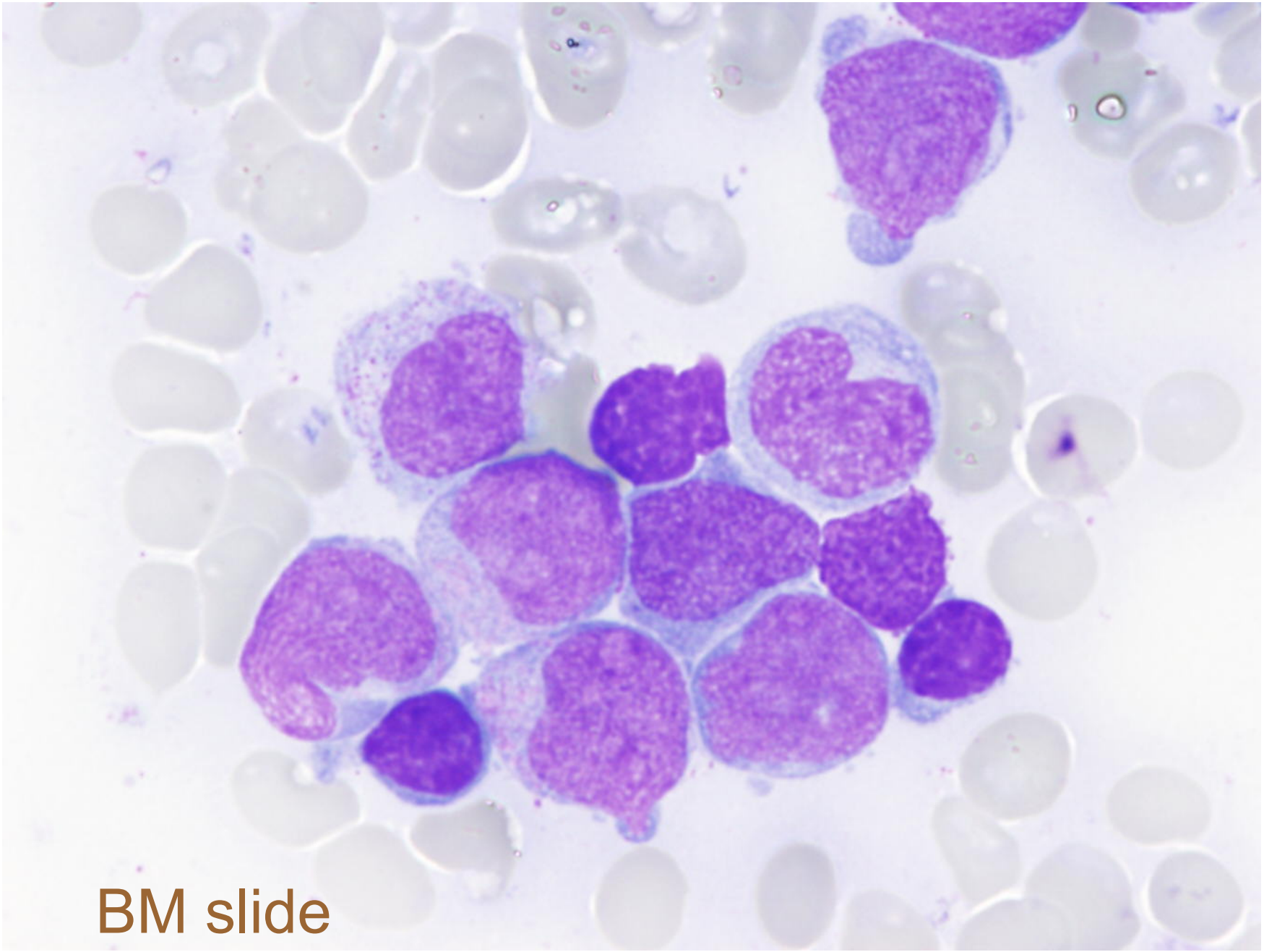
Clinical report (I)

- 42-yr old woman
- Recipient of a liver transplant due to VHB & VHD 4 years ago
- On-going immunosupression with “low-dose” tacrolimus
- Incidental finding of leukocytopenia 1 month ago
- Asymptomatic

Lab results

- Hb 11.5 g/dL WBC 3.7 x 10^9/L (38 N/2 NS/9 E/27 L/12 M/12 blast cells) Plt 45 x 10^9/L
- GGT 50 U/L LDH 512 U/L
- Prothrombin t 75% APTT 34'' FDP (+)


PB slide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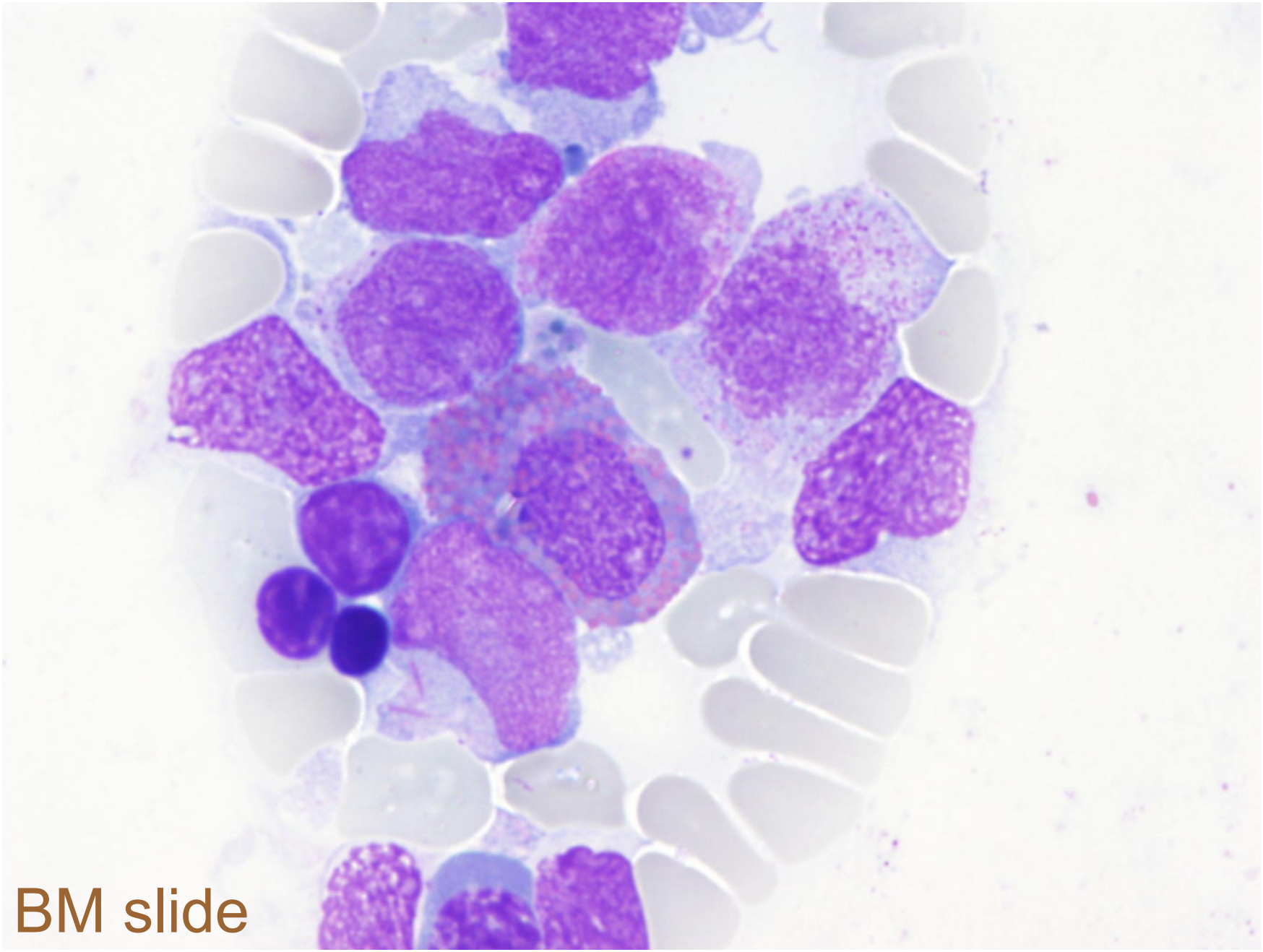
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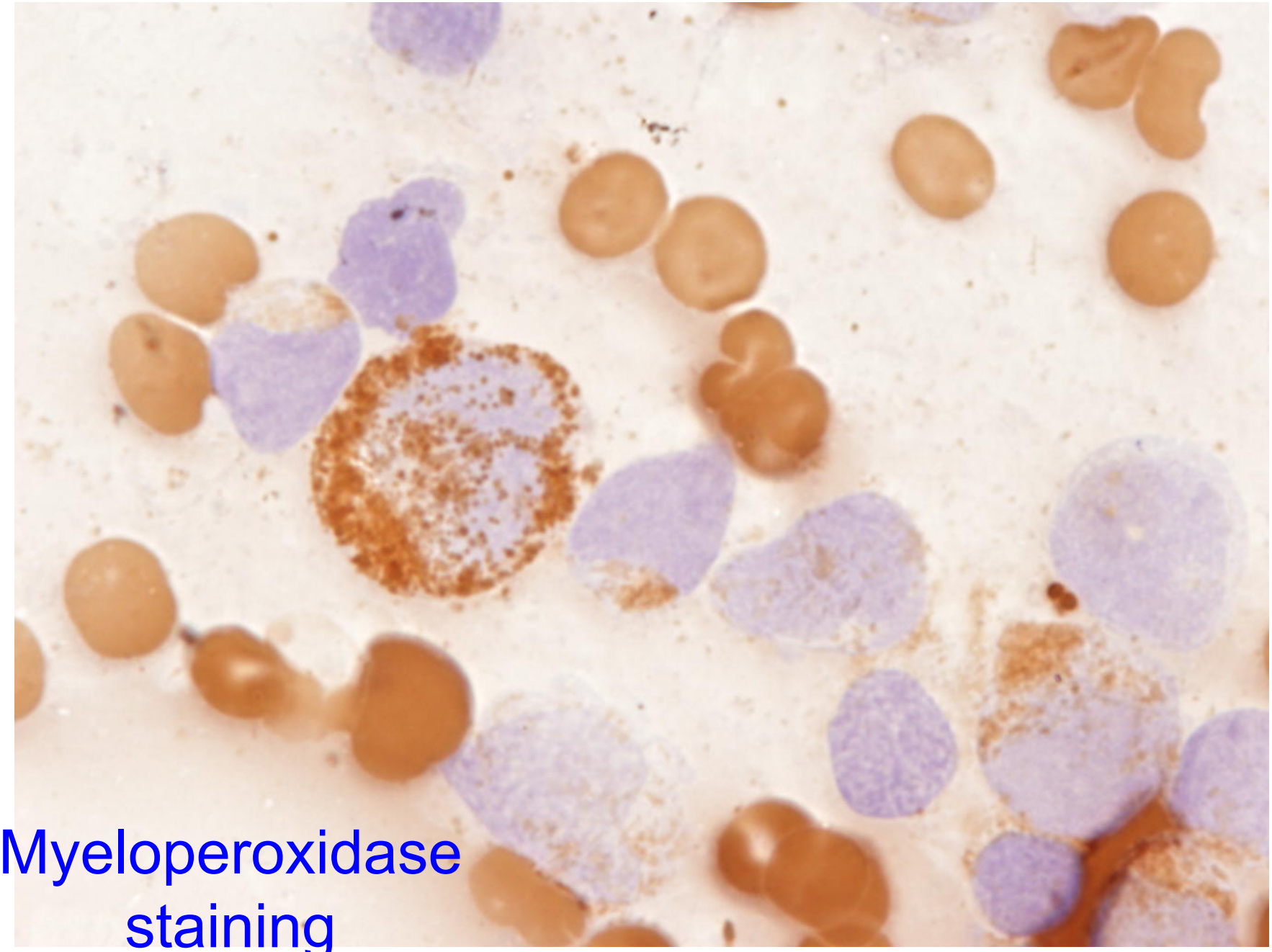
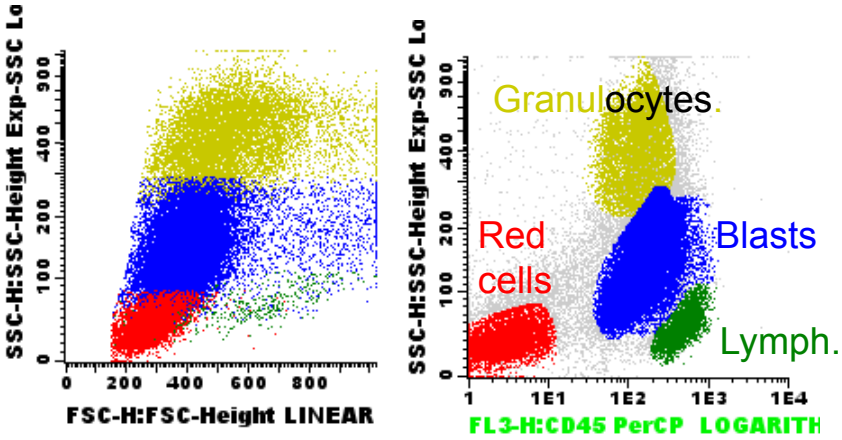
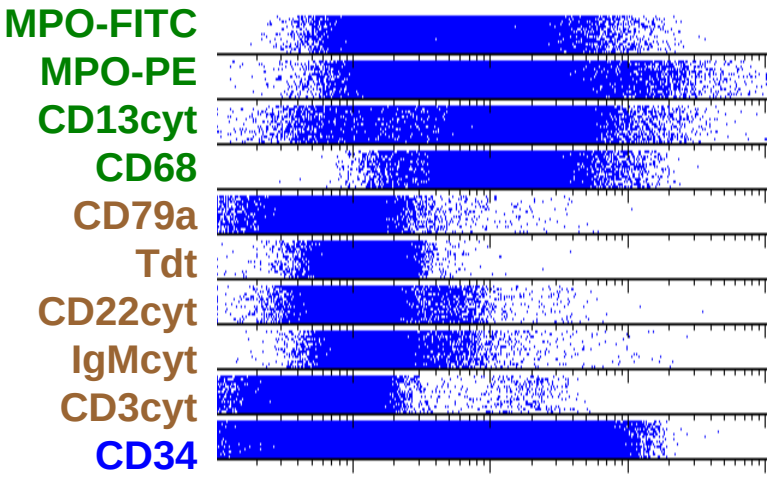
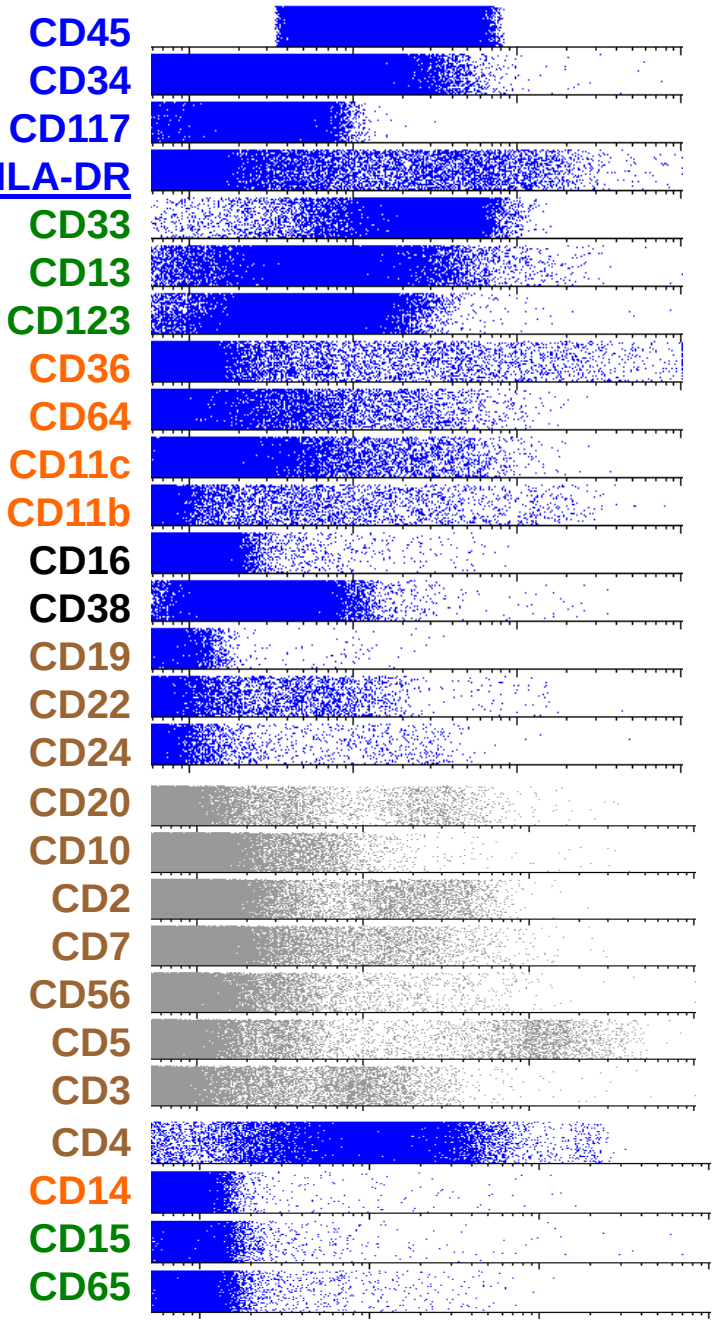


Myeloperoxidase staining



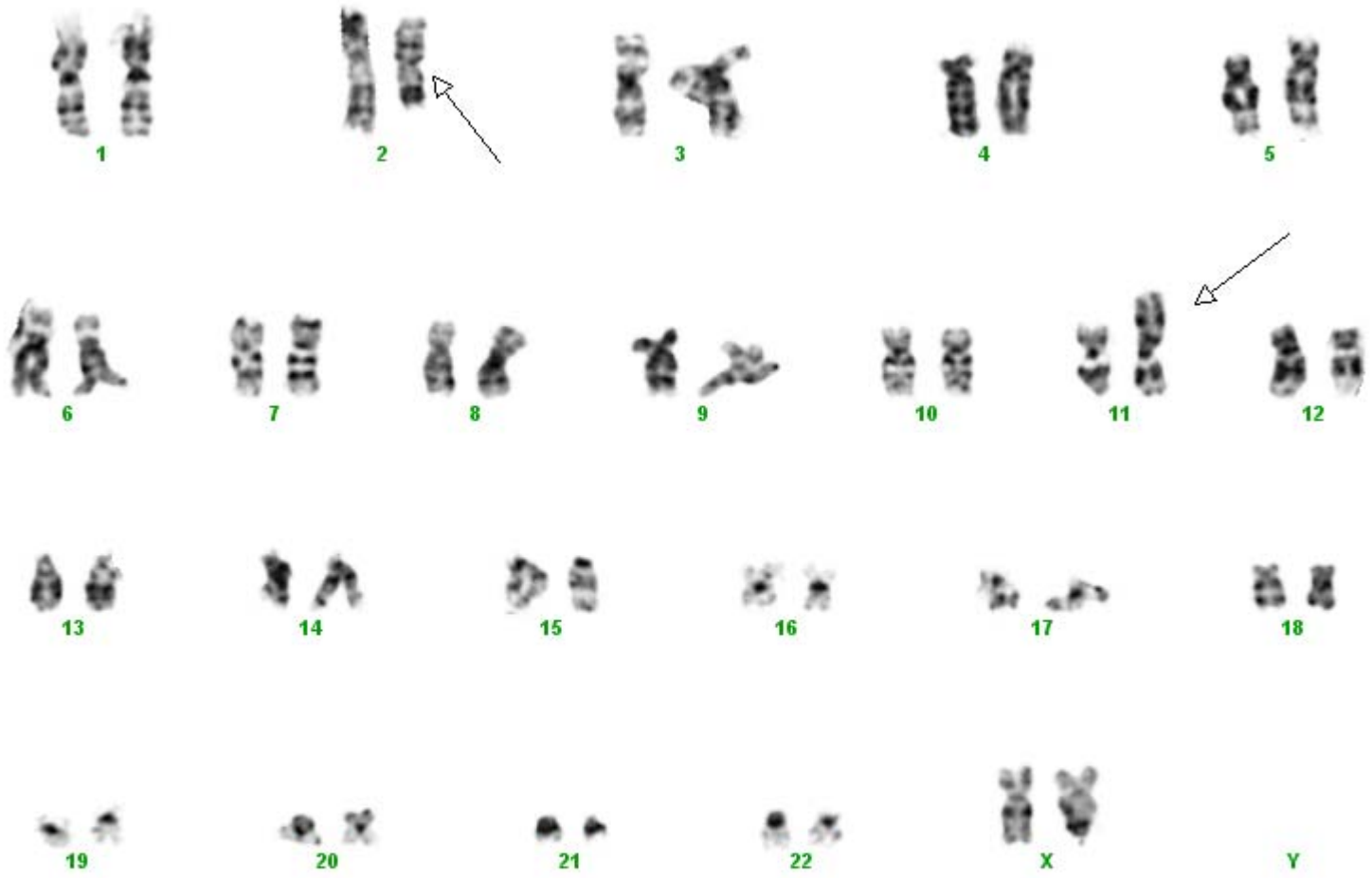




Phenotype of blasts (49%):

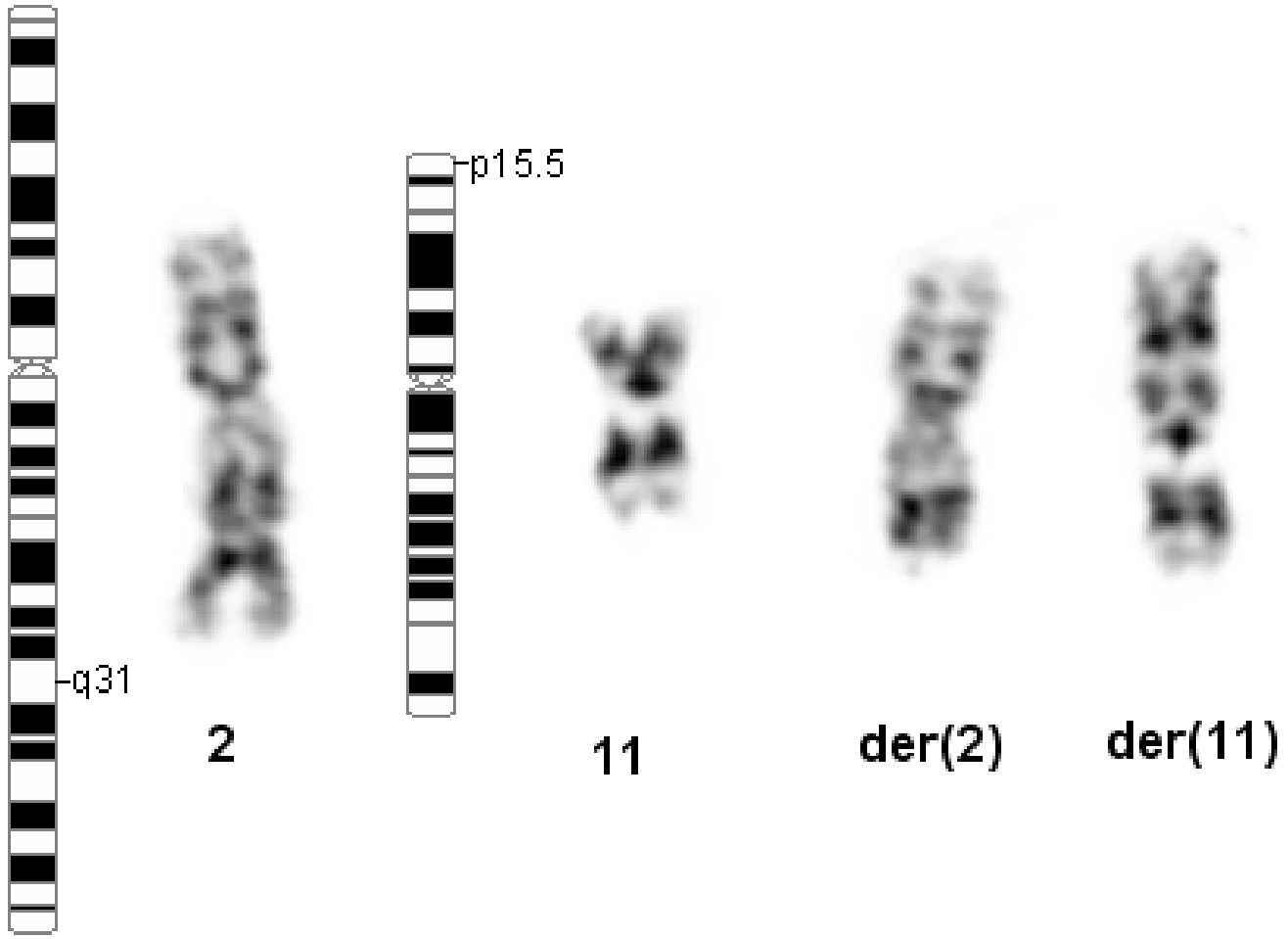
$CD34^{partial}$ $CD45^{dim}$ CD117+ **HLA-DR-**
CD13+ CD33++ CD123+ MPO+
CD36- CD64- CD4+ CD11b- CD11c± CD14-
CD15- CD65- CD16-
Lymphoid B, T & NK neg

Karyotyping (BM)

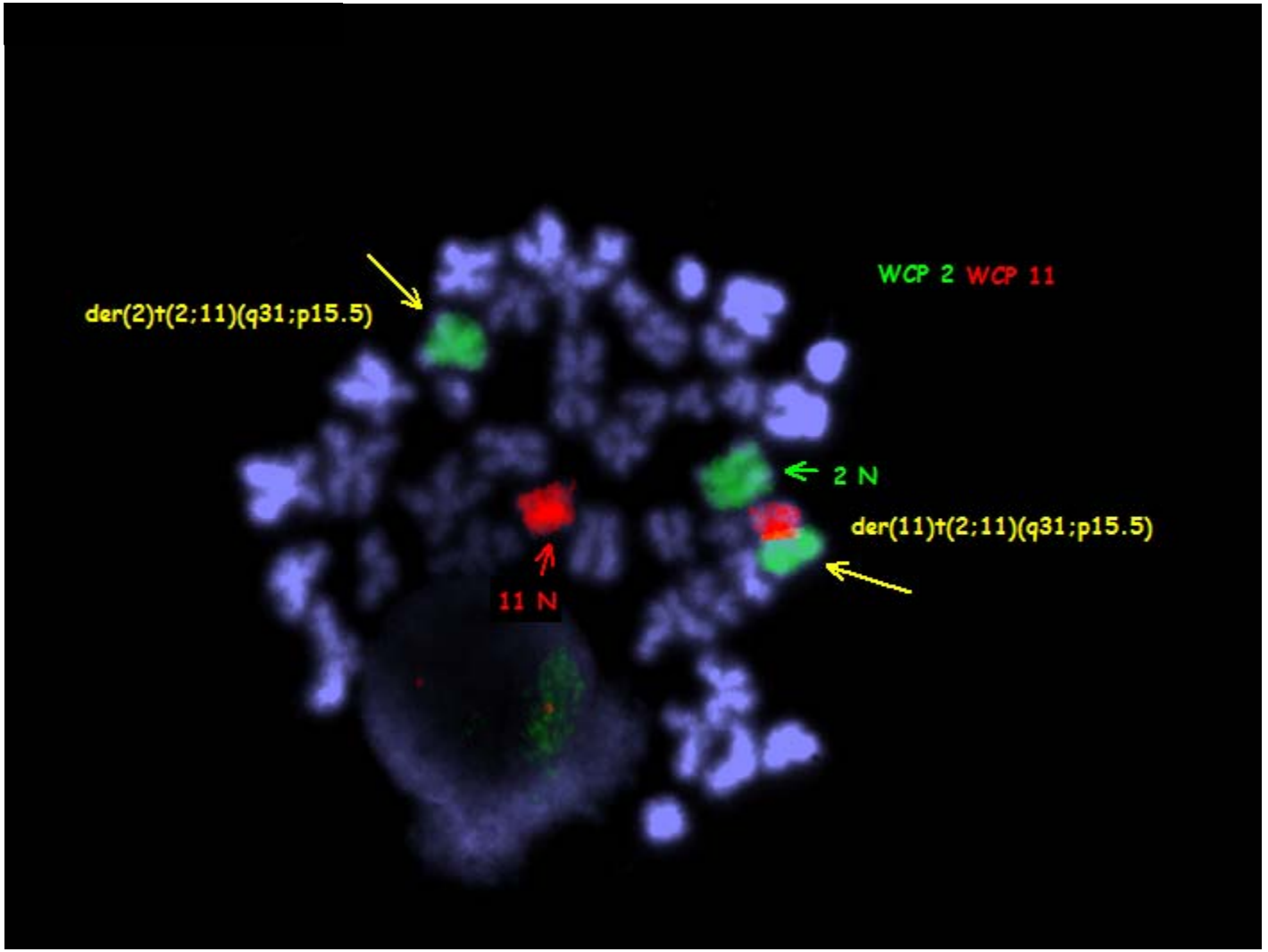


46,XX,t(2;11)(q31;p15)

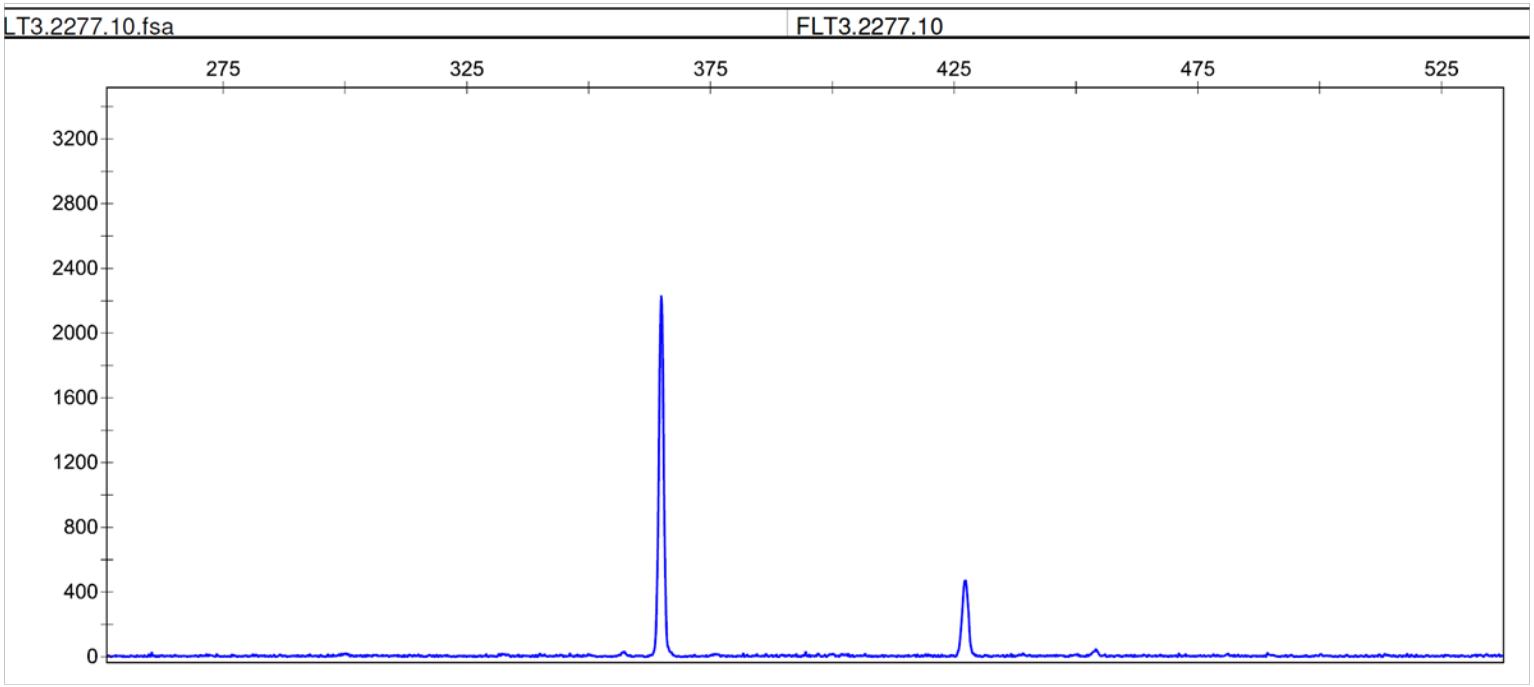
Translocation t(2;11)(q31;p15): scheme



FISH analysis: whole chromosome painting of chromosomes 2 & 11



PCR FLT3 gene



AUC 20111 5083

Ratio FLT3-ITD/wt = 0.25

Additional molecular screening

- Absence of PML-RARα, RUNX1-RUNX1T1 & CBFβ/MYH11 rearrangement
- Absence of NPM1 mutation
- Chimerism analysis (STR-PCR) of a hair & bone marrow sample: identical microsatellite pattern

Integrated diagnosis

- Acute myeloid leukemia with myelodysplasia-related changes (MRD) - *WHO 2008-based*
- AML with MRD & FLT3-ITD – *operative/prognostic diagnosis*
- AML with translocation t(2;11)(q31;p15) & NUP98-HOXD11/HOXD13 rearrangement, with FLT3-ITD - *comprehensive diagnosis, not yet in WHO 2008, but to be included in next WHO classification* … in a liver transplant recipient - *with clinical information/* recipient's origin

Evolution

INDUCTION (IDICE-G)

CR

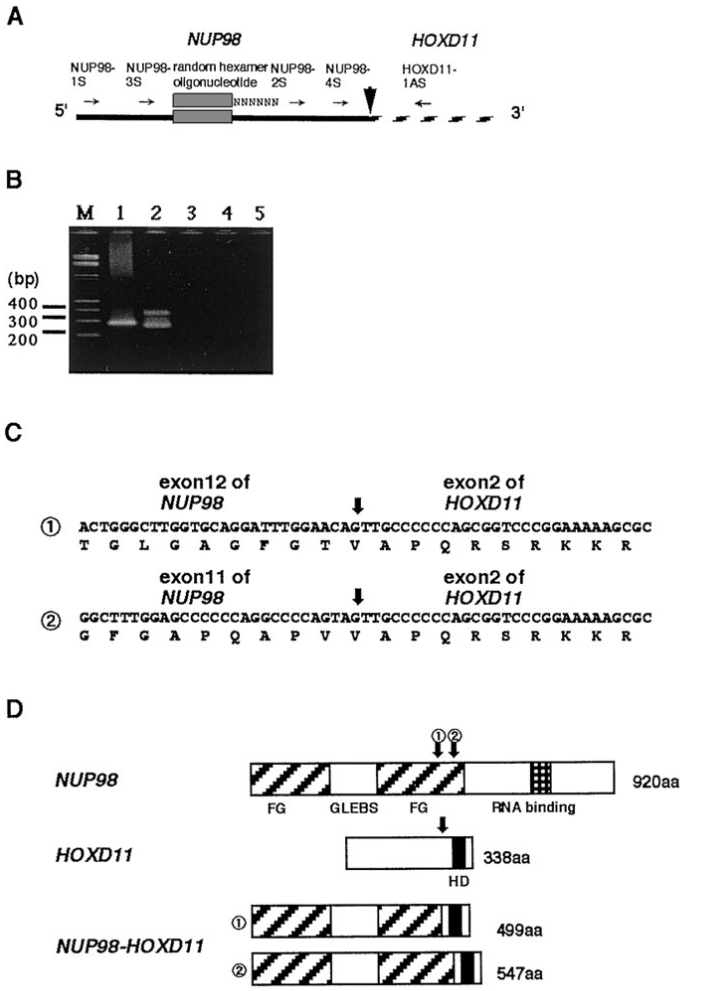
INTENSIFICATION (MTZ+HIDAC)

?

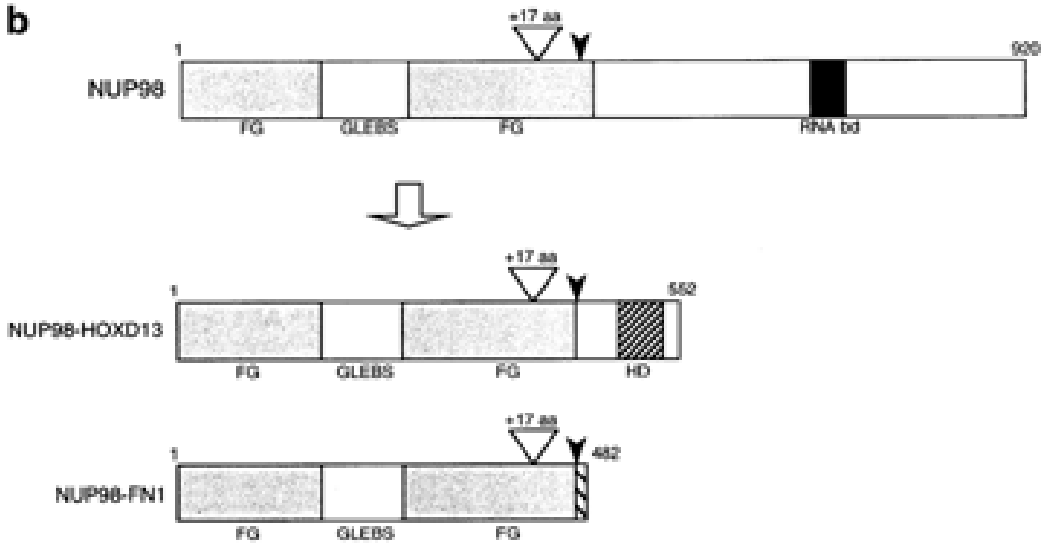
Issues to be raised

- AML with NUP98 rearrangement universe
- AML in liver transplant recipients
- Clinical management!

AML with t(2;11)(q31;p15): fusion gene products



NUP98/HOXD11 fusion gene



NUP98/HOXD13 fusion gene

AML with NUP98 rearrangement: an universe with multiple partners

- NUP98 (11p15): a nucleoporin involved in RNA transport from nucleus → cytoplasm
- Translocation of NH2-portion of NUP98 protein to ≥9 different partners
- Partners: HOXA9 (7p15); HOXD13 & HOXD11 (2q31) TOP1 (20q11); *DDX10-dead box RNA helicase* (11q22); JARID1A-*Rb-binding protein 2* (12p13);…

AML with NUP98 rearrangement: clinical features

- Presenting either as *de novo* or therapy-related AML (topo-II inhibitors), MDS, BC-CML
- Several reports from Eastern population
- Predominance in children & young adults
- Diverse phenotype (M2, M4, M7, …)
- Aggresive course different partners

AML in liver transplant recipients

- <20 cases reported – increased incidence among liver transplant recipients suggested
- Variable interval livex Tx - AML
- APL as most frequent entity!
- Two reported cases of donor origin
- AML as a transplant/immunosupression-related disease?
- Standard management of AML have lead to an adequate disease control in some of these pts

Clinical management: how to proceed?
(*your contribution is highly appreciated*)

- High-risk AML (NUP98-r AML, FLT3-ITD): candidate to allogeneic HSCY
- AlloHCT in a liver transplant recipient? Allogeneic HSCT as a platform for organ tolerance
- Design of an “ad hoc” minimal residual disease strategy for molecular follow-up

Unitat d'Hematopatologia from Hospital Clínic*: the integration team*