



# 8<sup>th</sup> SYMPOSIUM ON **Acute Promyelocytic Leukemia**

*Dedicated to Prof. Francesco Lo Coco*

*Featuring an AML meeting coordinated by **EHA** SWG AML*

**10-11 Aprile 2024**

**ROMA** • Hotel NH Collection Roma Centro



# “Genotypic and phenotypic features of APL-like AML”

*Francesco Buccisano*

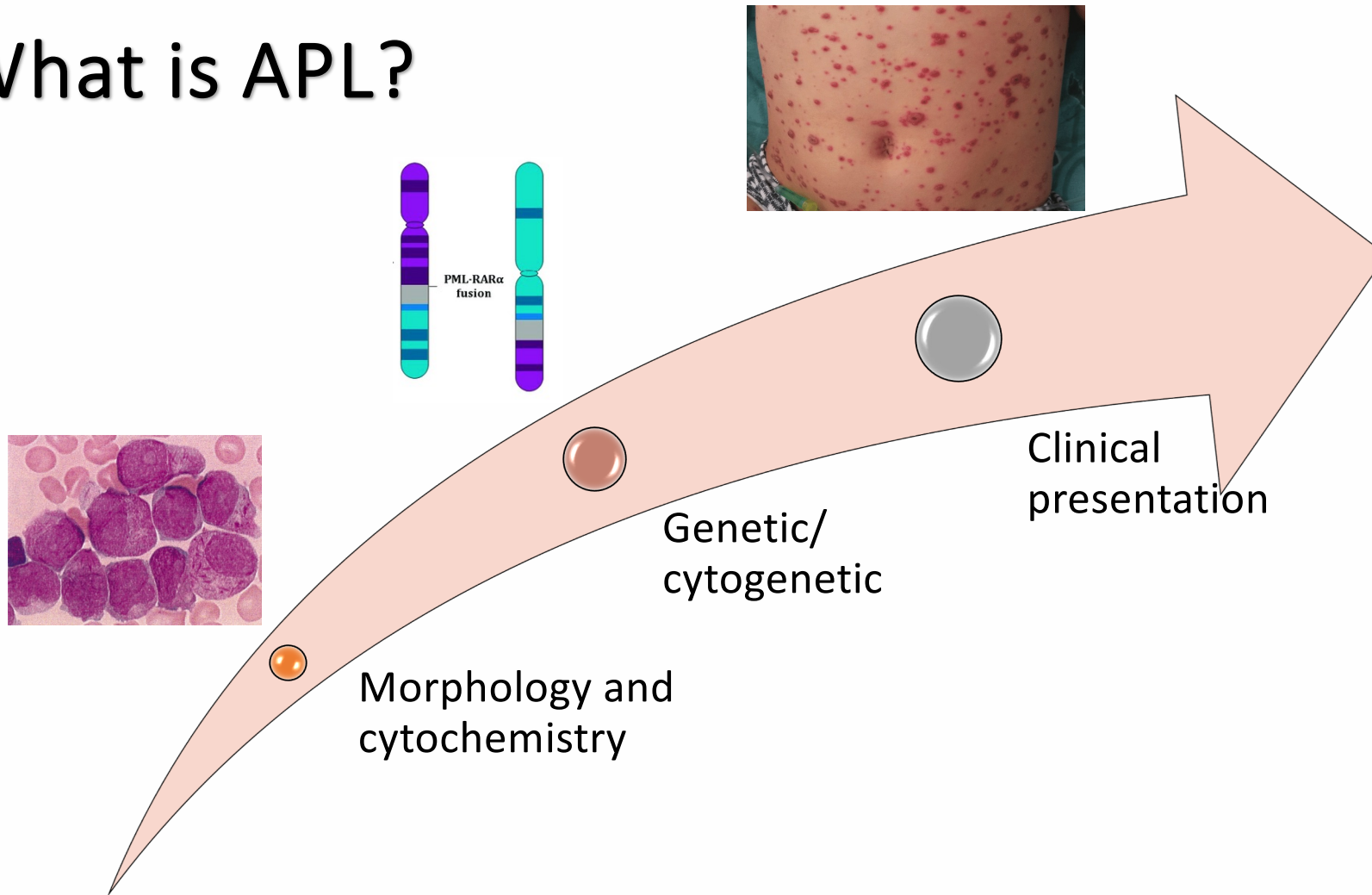


## Disclosures of Francesco Buccisano

Company name	Research support	Employee	Consultant	Stockholder	Speakers' bureau	Advisory board	Other
JAZZ PHAMACEUTICALS			X				
NOVARTIS			X				
LABORATORIES DELBERT						X	
ABBVIE						X	
BRISTOL MEYERS SQUIBB					X		
JANSSEN-CILAG					X		
ASTELLAS					X		
MENARINI STEMLINE					X		



# What is APL?



# Acute Myeloid Leukemias M2 Potentially Misdiagnosed as M3 Variant French-American-Britain (FAB) Subtype: A Transitional Form?

SUSANNA FENU,\* DANIELA CARMINI,\* FRANCESCA MANCINI,\* CESARE GUGLIELMI,\*  
GIULIANA ALIMENA,\* ROBERTA RICCIONI,\* PAOLA BARSOTTI,† MARCO MANCINI,\*  
GIUSEPPE AVVISATI\* and FRANCO MANDELLI\*

\*Haematology, Department of Human Biopathology; †Section of Ultrastructural Pathology, Department of Experimental Medicine,  
University "La Sapienza", Rome, Italy

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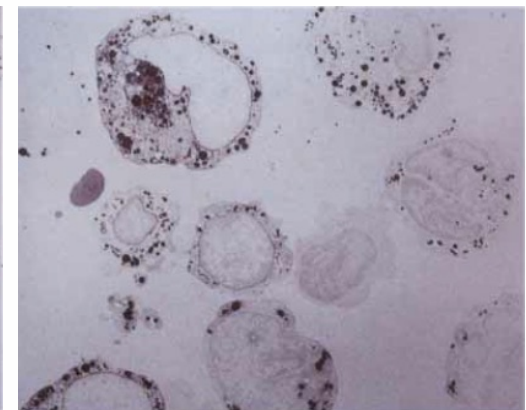
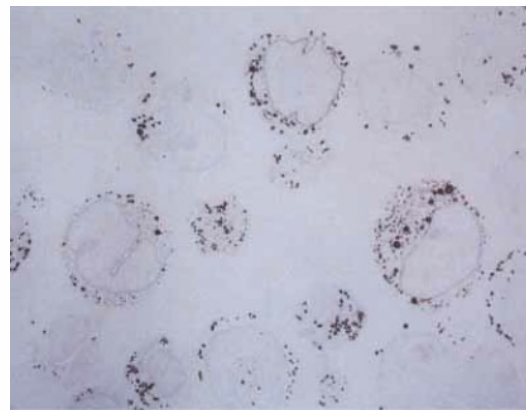
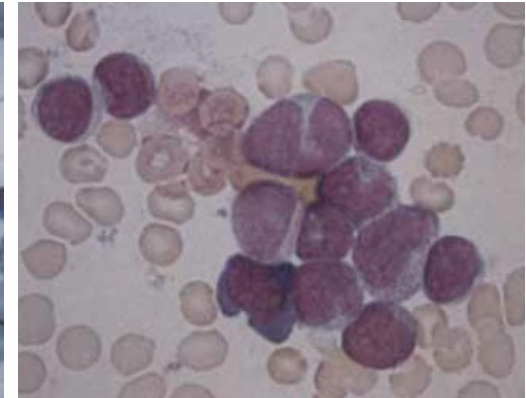
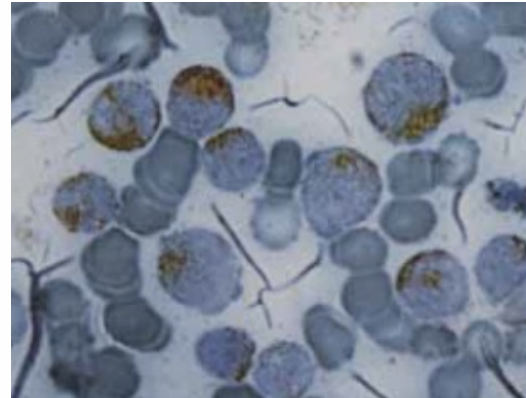
Immunophenotype showed HLA-DR-, CD13+, CD33+, CD2+, CD9+ promyelocytic features were also detected by electron microscopy.



However, leukemic cells lacked both translocation t(15;17) and PML/RARa gene rearrangement.



“The atypical M2 subtype may be confused with the M3v if only cytochemistry, immunophenotype and electron microscopy are used in the defining the FAB subtypes”.



Fenu S et al, Leuk and Lymph 1995

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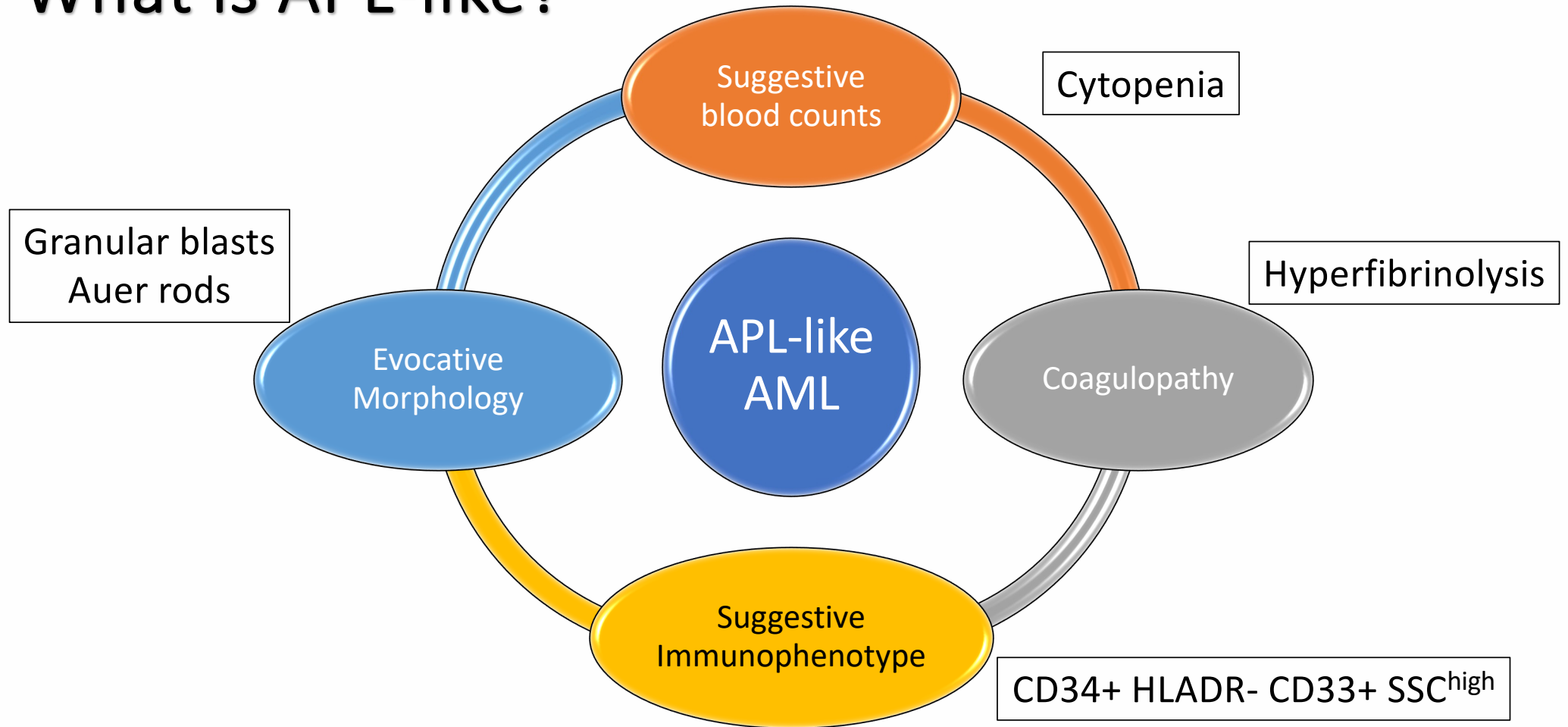
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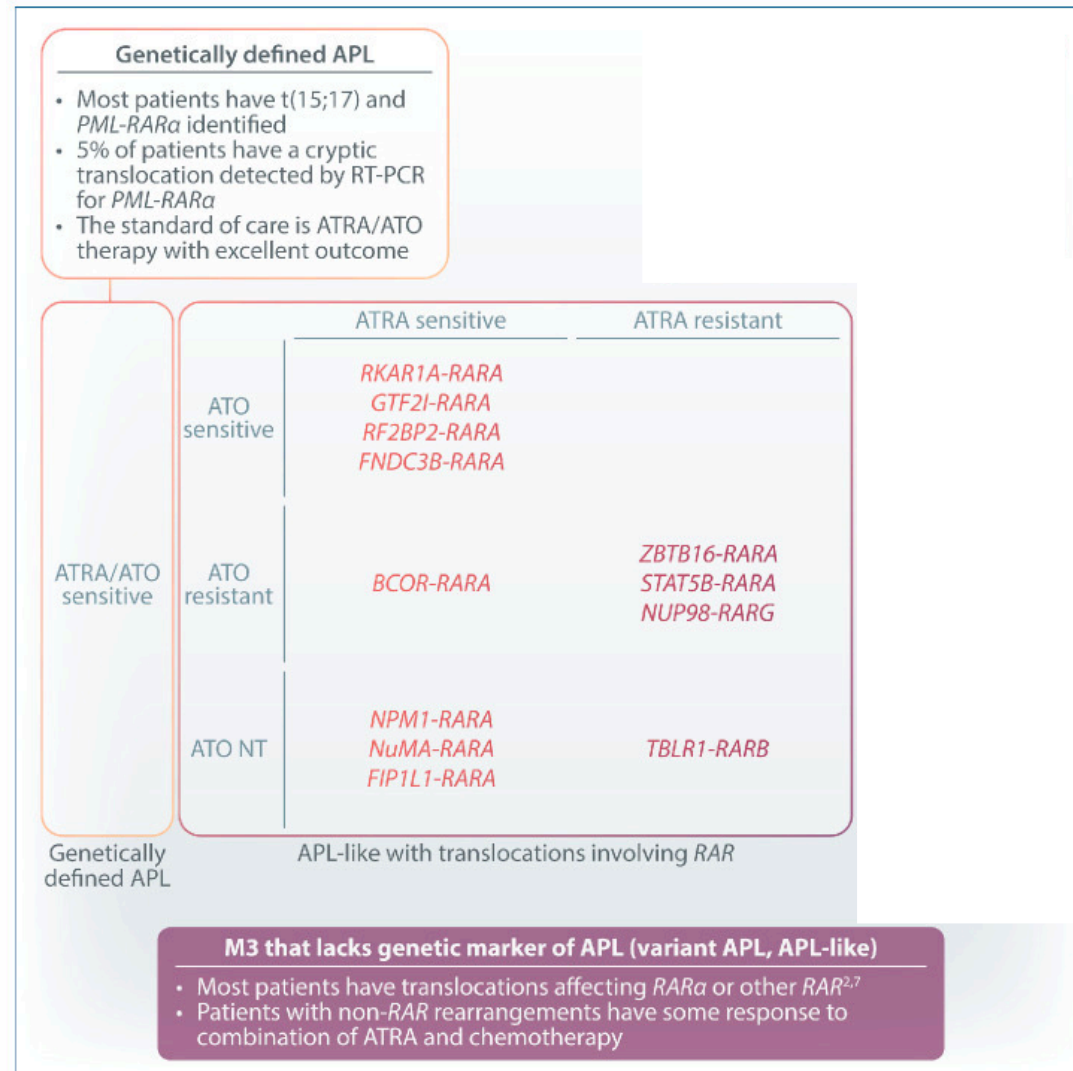
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# What is APL-like?



# The enigmatic cousins of APL...

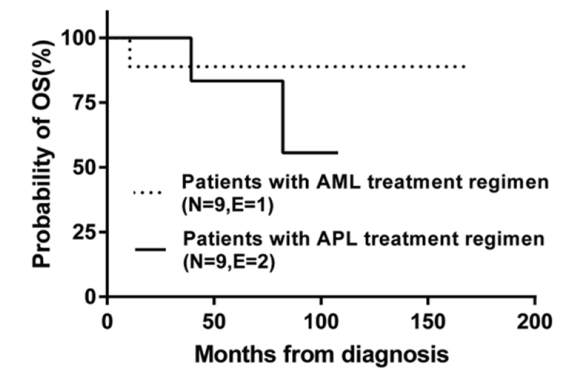
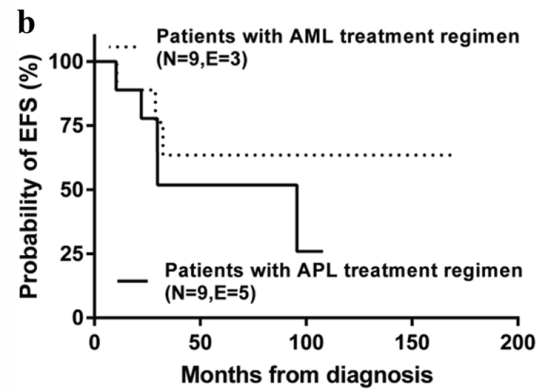
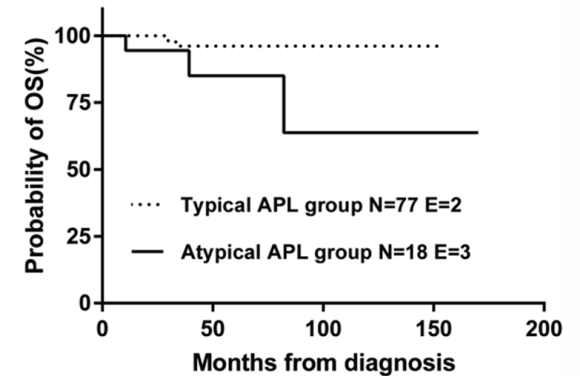
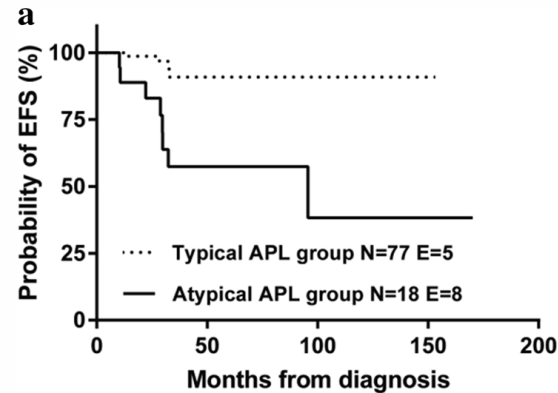
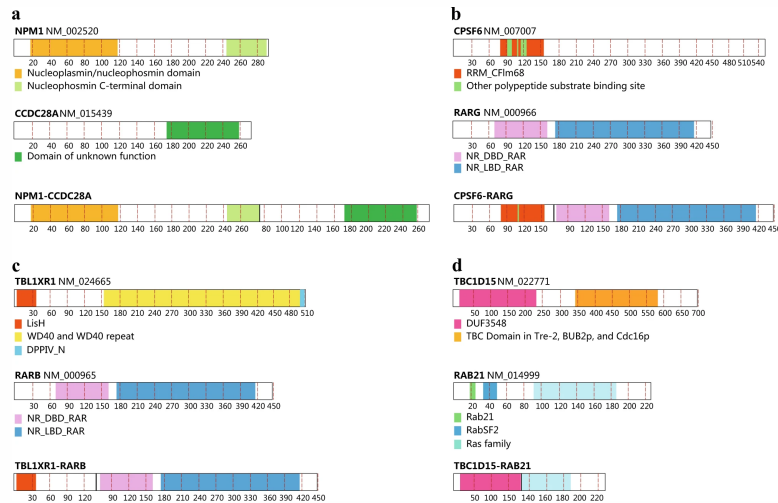


A. Ghiaur & G. Ghiaur, Haematologica 2023



# APL-like with translocations involving RAR

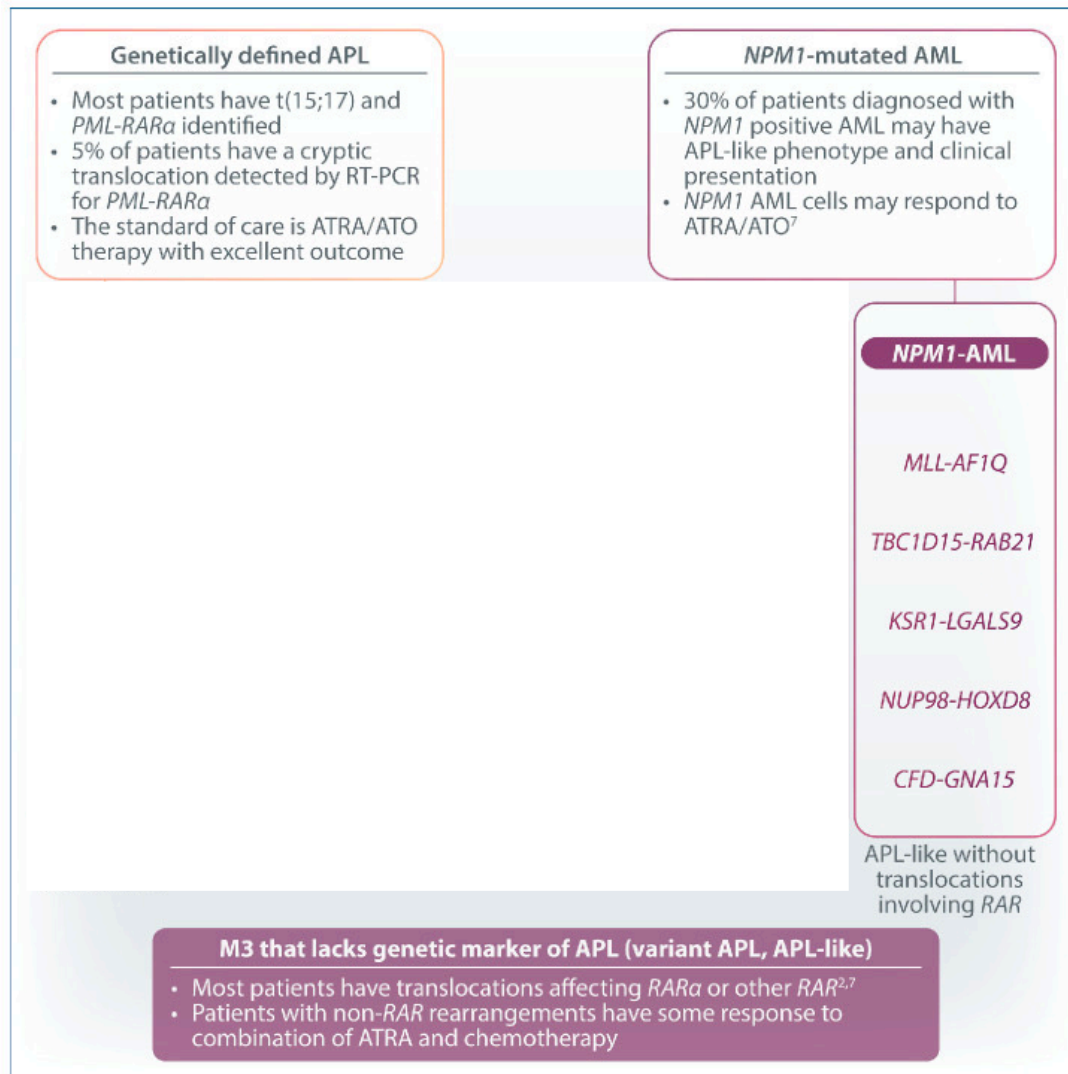
- 136 pediatric patients diagnosed with APL by morphology and MFC
- DNA samples available
- 24/119 (20%) negative for RARA rearrangements by multiple techniques



Zhao J et al., Leukemia 2018



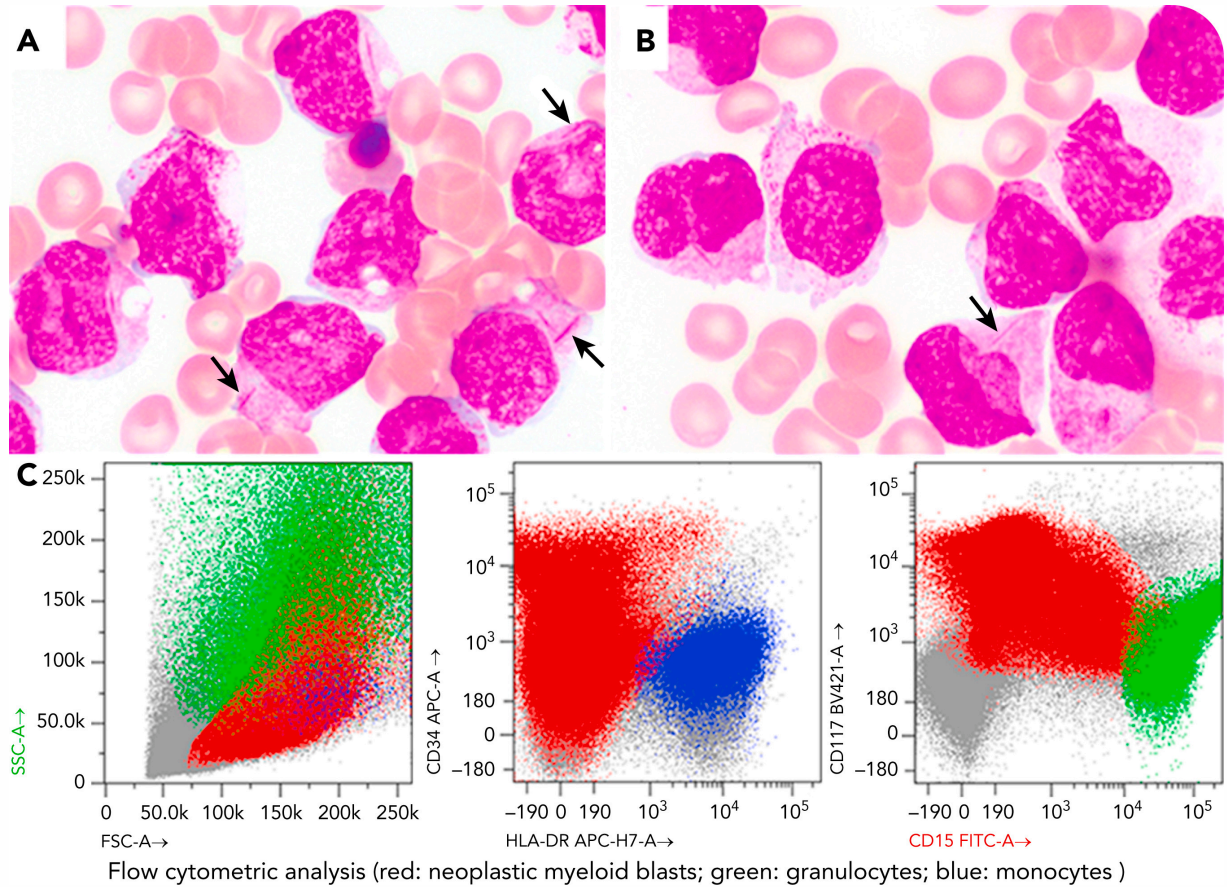
# The enigmatic cousins of APL...



A. Ghiaur & G. Ghiaur, Haematologica 2023



Acute myeloid leukemia with NUP98::HOXA9 mimicking acute promyelocytic leukemia



Lin & Wang, Blood 2023

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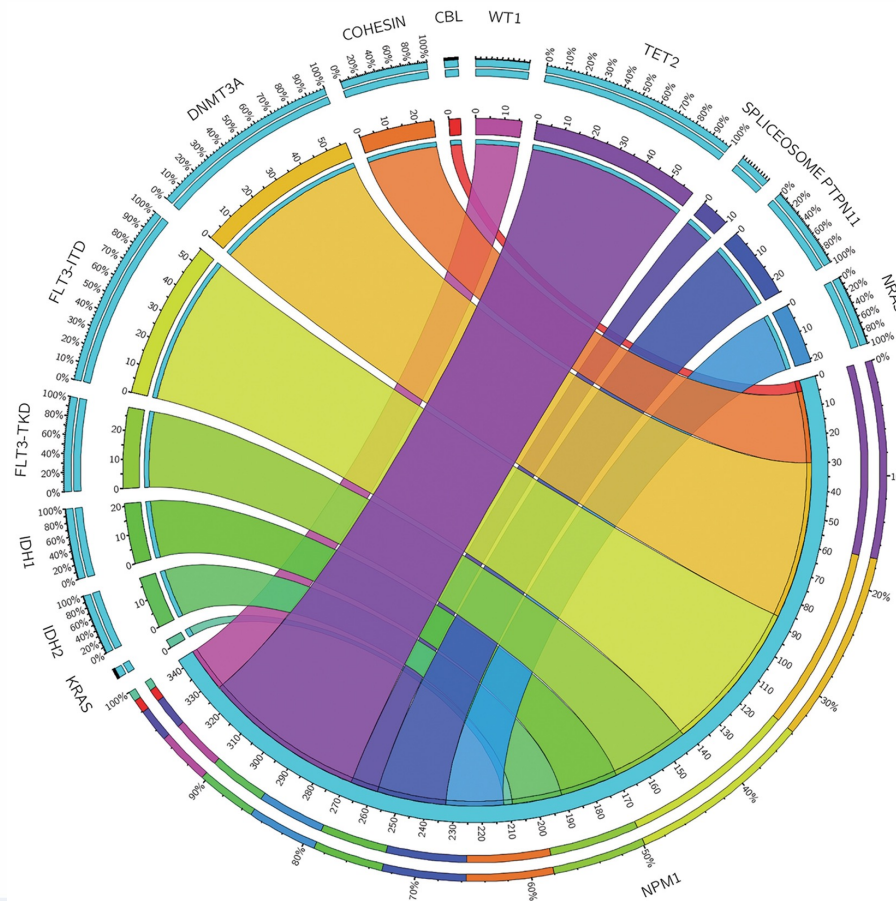
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# NPM1-mutated AML



Ptel JL et al., Leuk Res 2017

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Mason EF et al, American J Hematol 2017

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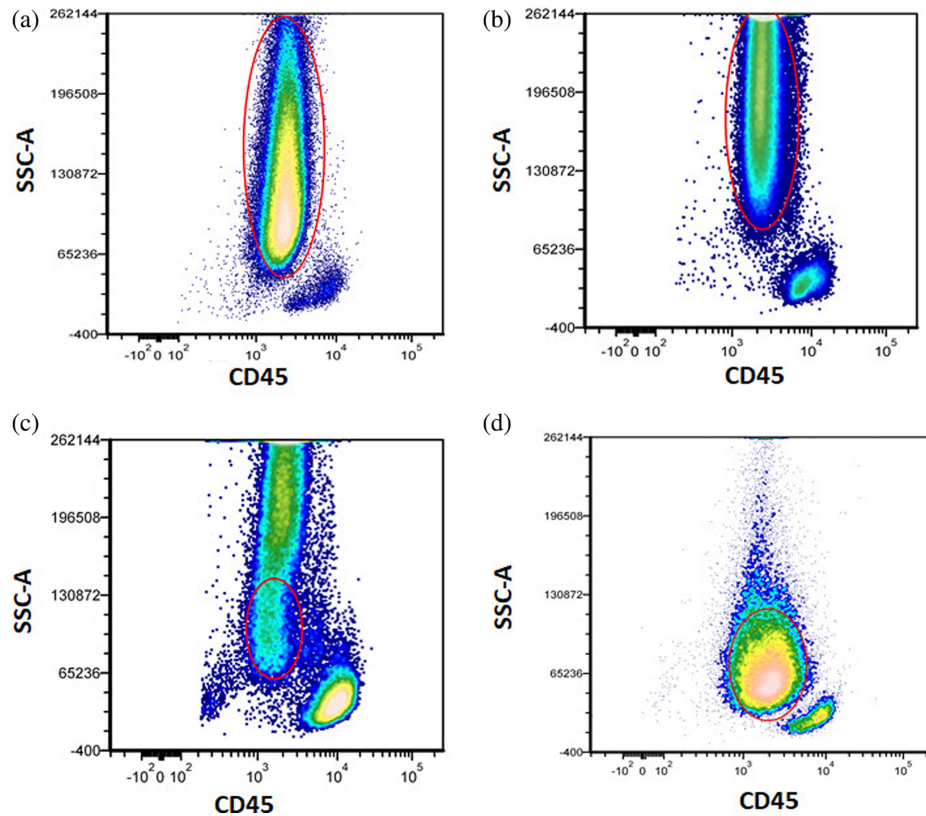
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# APL-like immunophenotype



- Pattern A-C (72%): typical APL
  - CD13+CD33+CD117+CD64+MPO+
  - CD34- HLADR-
- Pattern D (28%):
  - CD2+, CD34+
  - Microgranular variants
  - NPM1 mutated
  - KMT2A rearranged

Fang H et al., Cytometry B 2022





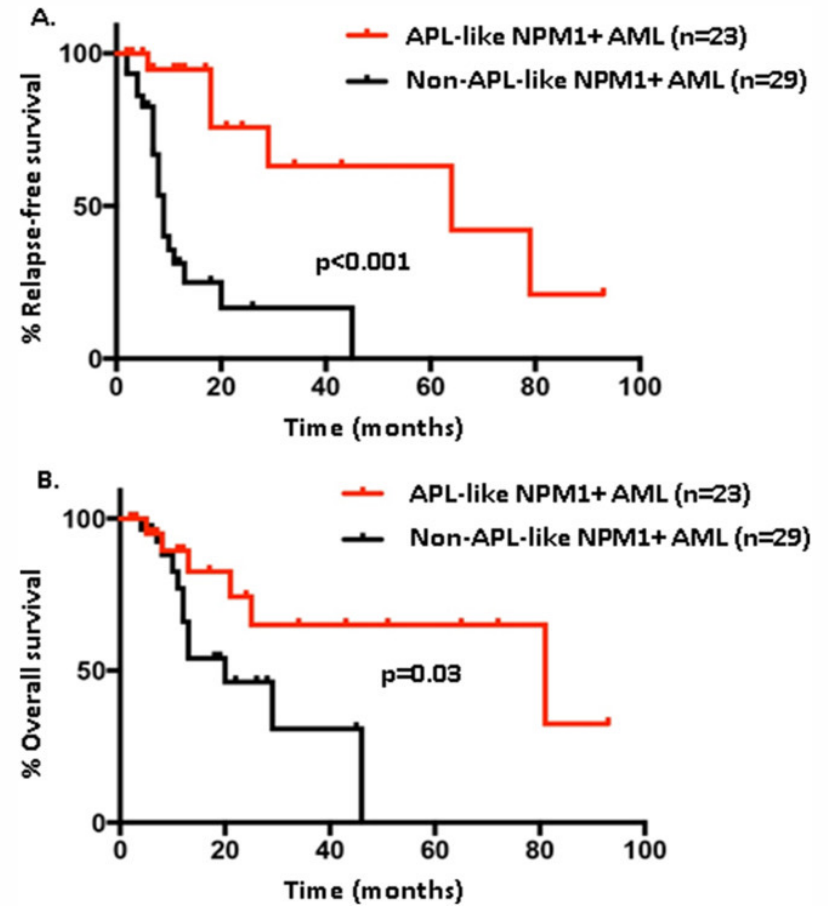
40/84 cases (48%) of NPM1-mutated myeloid AML cases demonstrate an APL-like immunophenotype



Co-mutations in TET2 or IDH1/2 are seen in nearly 100% (39/40) of such cases



Cases of NPM1-mutated myeloid AML with an APL-like immunophenotype are associated with improved outcome

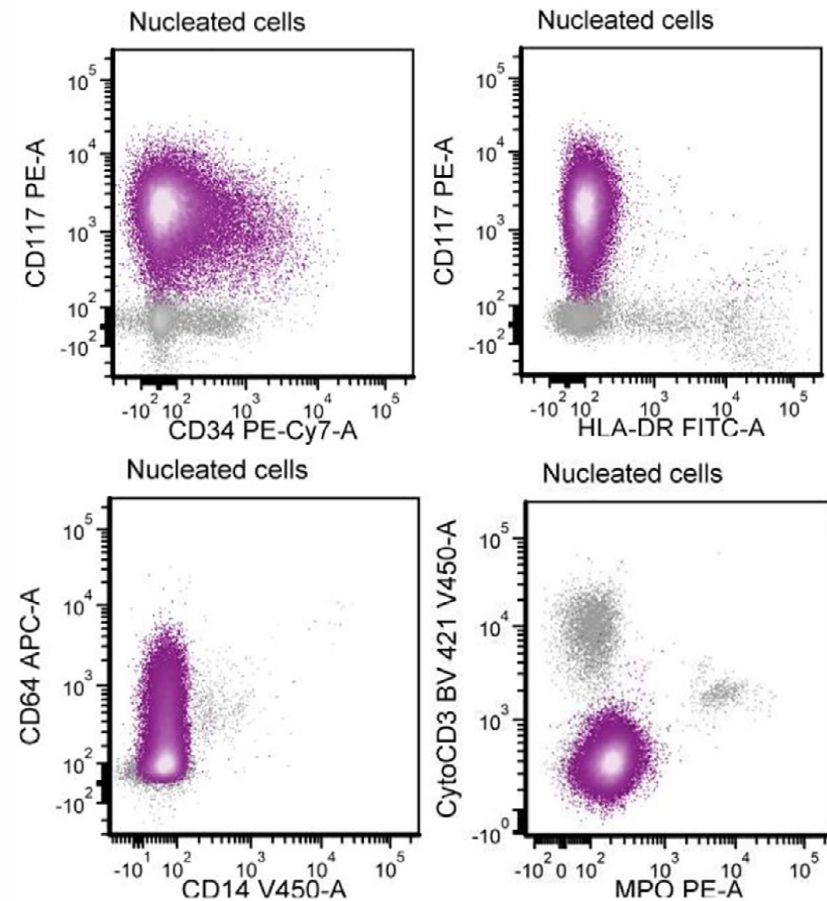
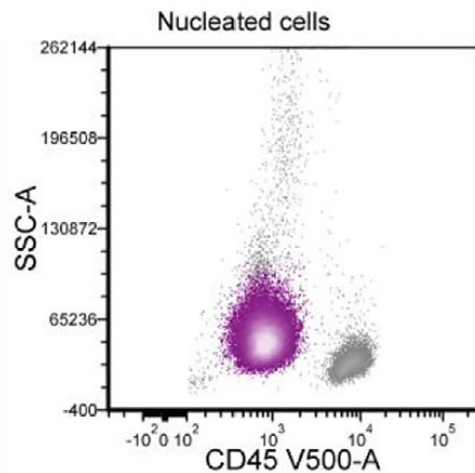


Mason EF et al, American J Hematol 2017



# AML with KMT2A (MLL) rearrangement

- 102 patients
- Five immunophenotypes: immature monocytic (38%); myelomonocytic (22%); myeloblastic (22%); mature monocytic (10%); and **APL-like (8%)**.

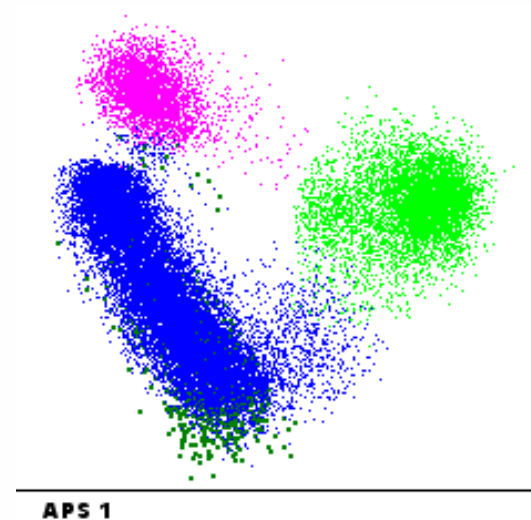
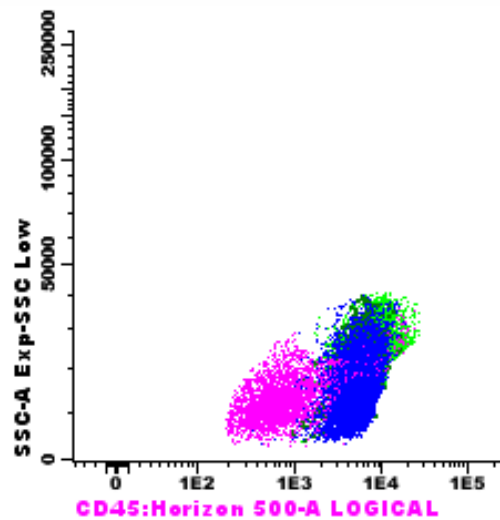


Konoplev S et al., Cytometry B 2022



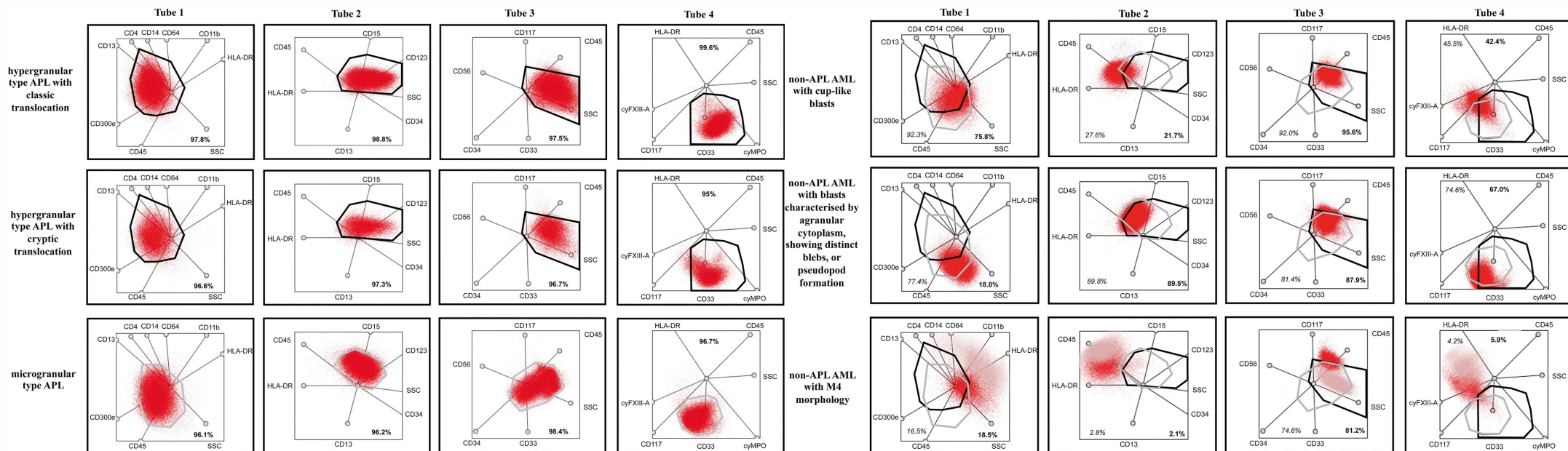
# Principal Component Analysis

- ✓ Automatic separation of the events, analyzing all the different choices of parameter combinations, based on Principal Component Analysis
- ✓ The parameters represented in these APS graphs are not a real measured parameter.





# Multidimensional plots for APL screening



Karai B et al., Annals Hematol 2019

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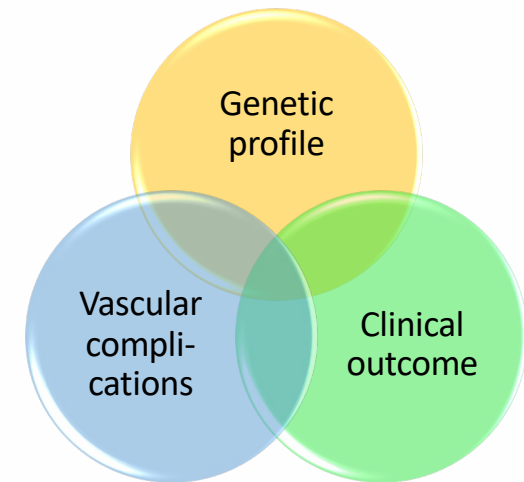
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# Conclusions

- ✓ Early identification of APL-like AML has practical implications
  - Timely non-APL treatment selection
  - Vascular complication prevention/treatment
- ✓ Genetics/cytogenetics represent the diagnostic gold standard
- ✓ Modern multidimensional MFC approach may speed up the diagnosis



Data on 207 APL-like patients presented by Crupi F...Mannelli F, 8<sup>th</sup> APL congress 2024

