9° WORKSHOP IN EMATOLOGIA TRASLAZIONALE

DELLA SOCIETÀ ITALIANA DI EMATOLOGIA SPERIMENTALE

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From Xenograft to Patient: The Impact of surface markers on AML Extramedullary invasion

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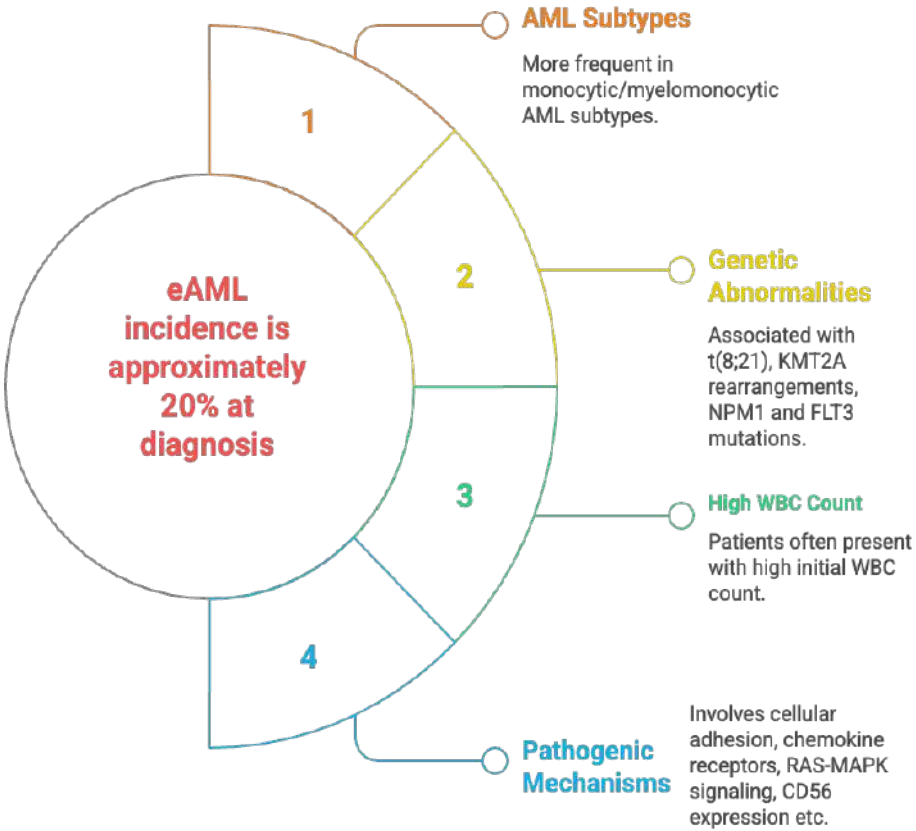
Disclosures di Matteo Caridi

No disclosures

Acute Myeloid Leukemia extramedullary invasion (eAML) represents a common disease feature



In Ganzel C et al. J Clin Oncol. 2016
Stölzel F et al. Haematologica. 2020
Shallis RM et al. Blood Rev. 2021

Multiple deregulated pathways contribute to the pathogenesis of eAML

ECM-Receptor Pathways

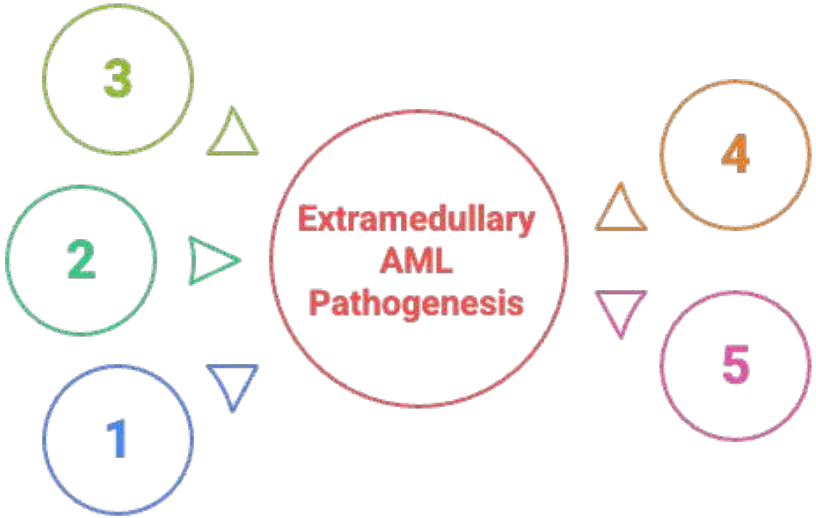
Supports tissue invasion and retention (dysregulation of focal adhesion pathways)

Chemokine Interactions

Guides AML cells to peripheral tissues (ex. CXCR4)

Cell Adhesion Molecules

Unusual expression promotes cell migration (ex. CD56)



EMT Pathways

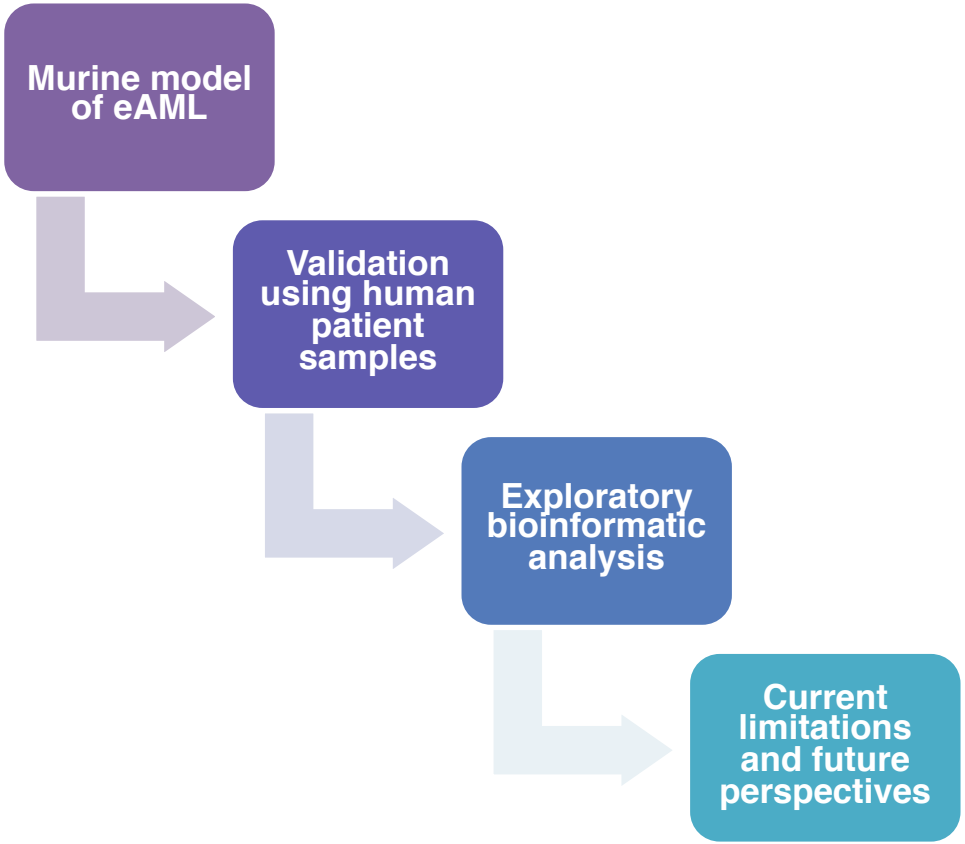
Mimics metastatic behavior and promotes infiltration

Matrix-Degrading Enzymes

Enhances invasive potential by degrading barriers

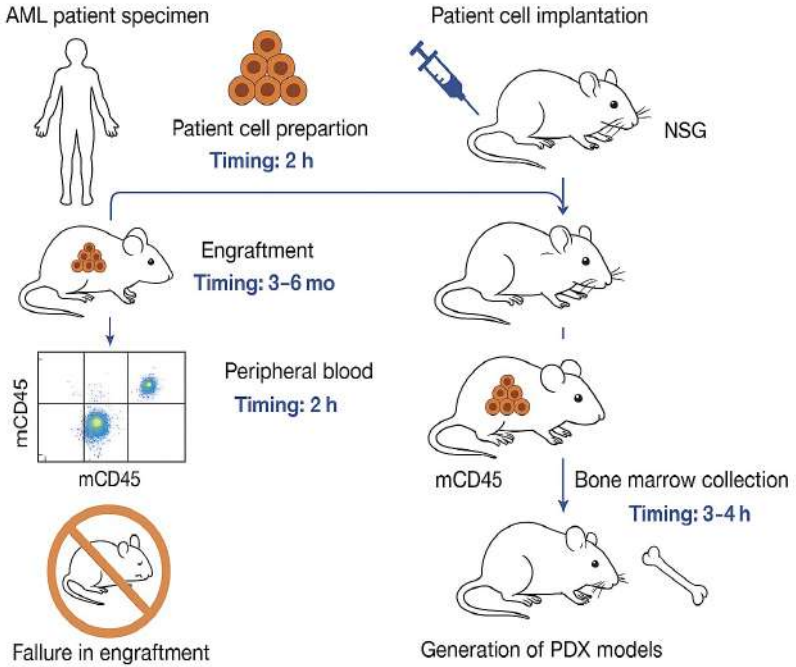
Ottone T et al. Leukemia. 2023
Shallis RM et al. Blood Rev. 2021

Materials and Methods: Workflow Overview



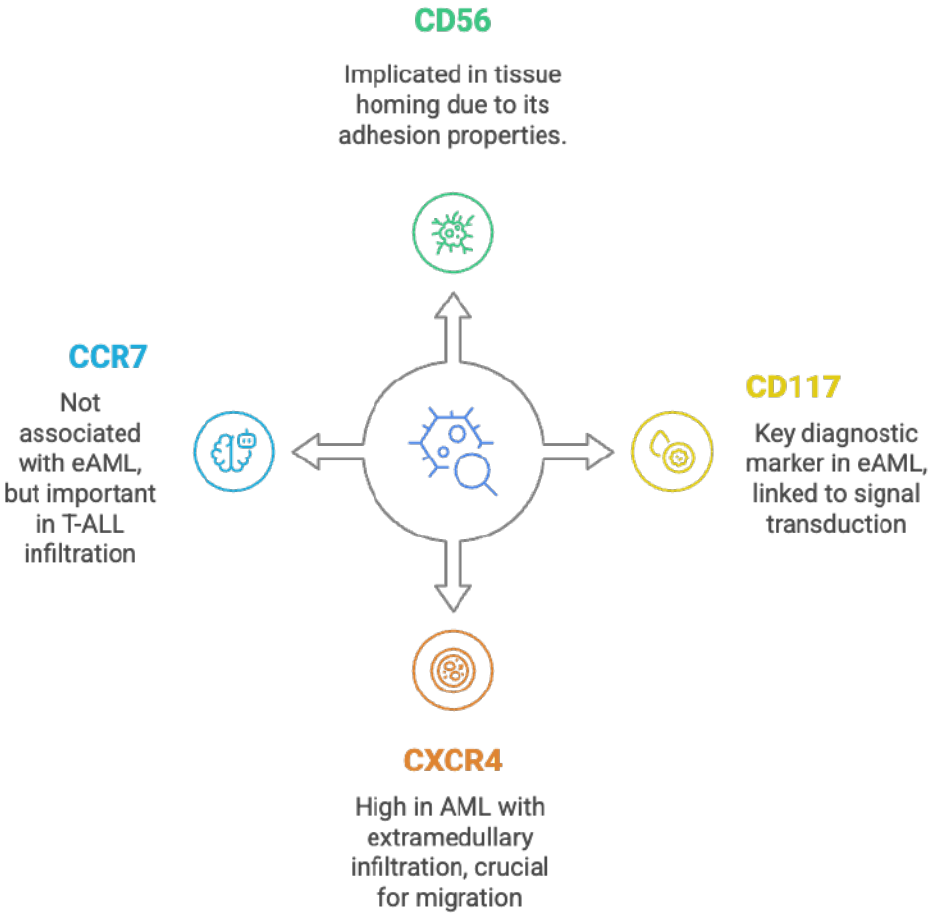
Establishing AML PDX Models: From Patient Cells to In Vivo Systems

- MNCs from AML patients are injected into IL-2Rγ-deficient NOD/SCID mice.
- Engraftment is monitored by CD45⁺ flow cytometry.
- Leukemic cells from P0 mice are serially passaged or cryopreserved to establish stable PDX models.

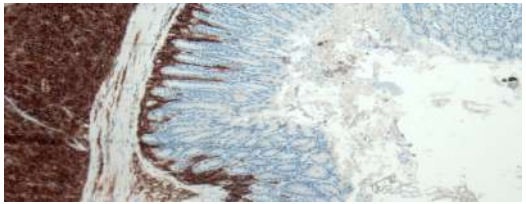


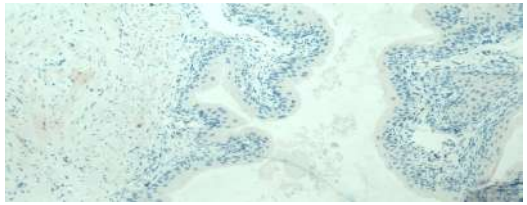
Adapted from N. Hassan et al. STAR Protocols 2020

Selection of selection of surface markers associated with extramedullary invasion in AML

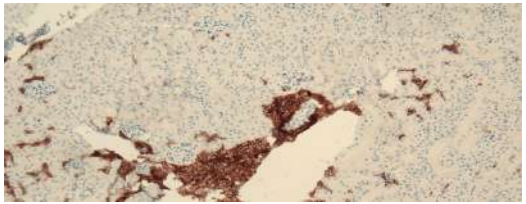


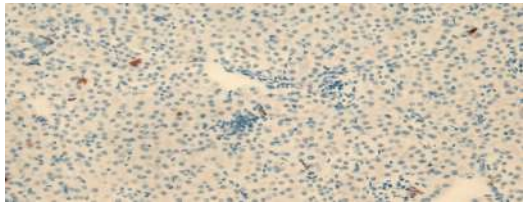
PDX derived from different patients display distinct extramedullary involvement (EMI)



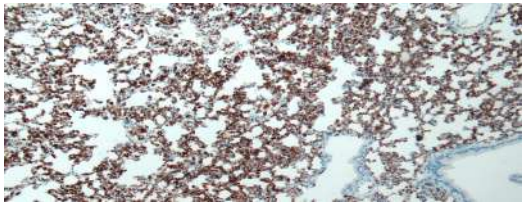


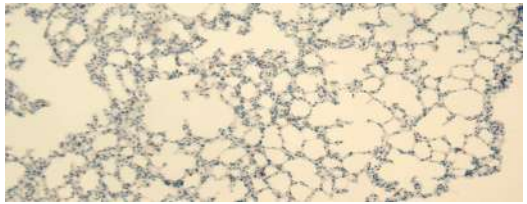
Gastric parenchyma





Renal parenchyma

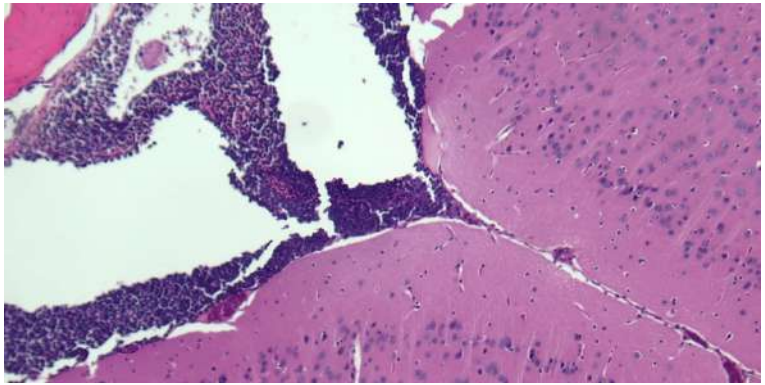


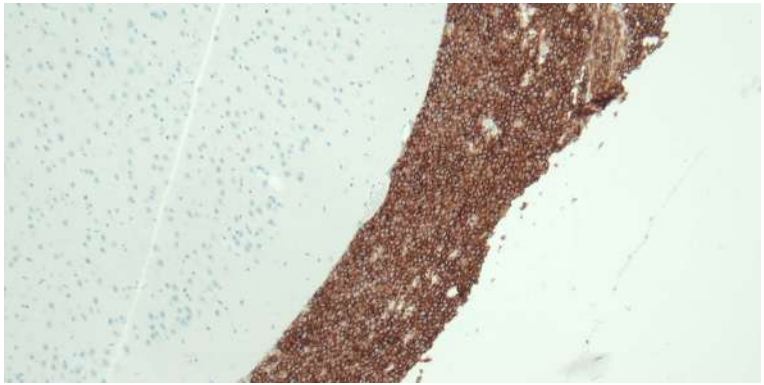


Pulmonary parenchyma

anti-human CD45 immunostaining 10x magnification

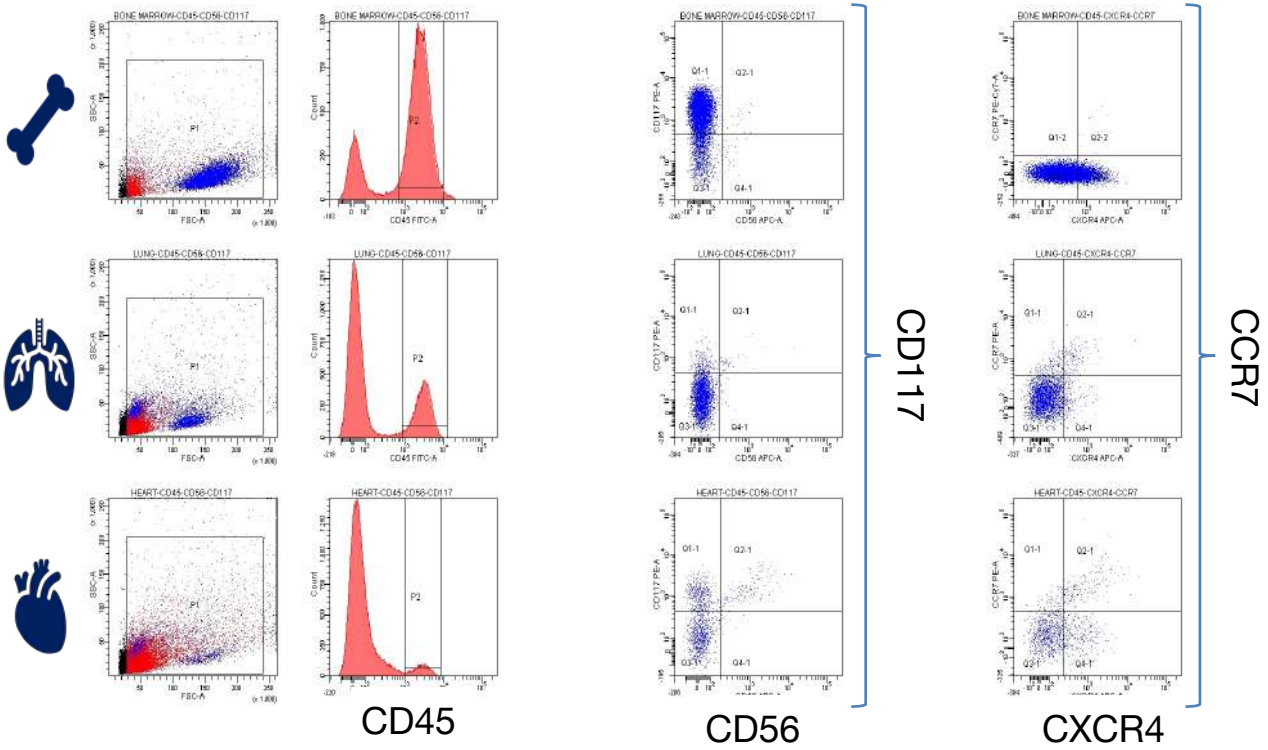
Predominance of meningeal involvement over parenchymal infiltration in the Central Nervous System





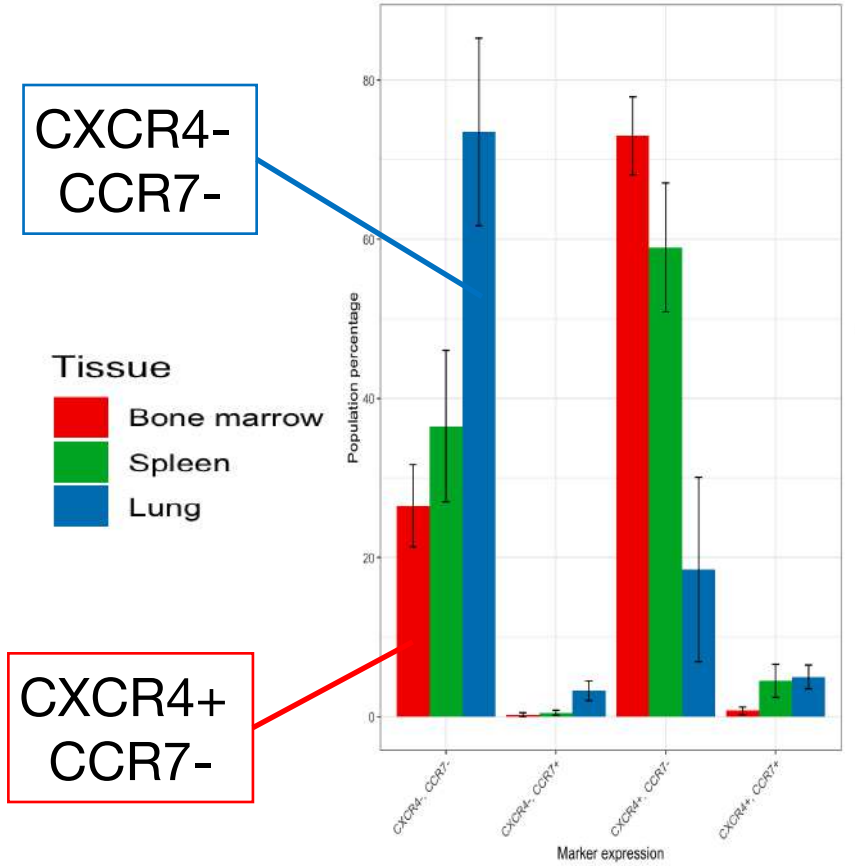
EE and anti-human CD45 immunostaining of CNS slices; 4x and 20x magnification respectively

Blasts isolated in different organs display distinct phenotype and homing receptors expressions

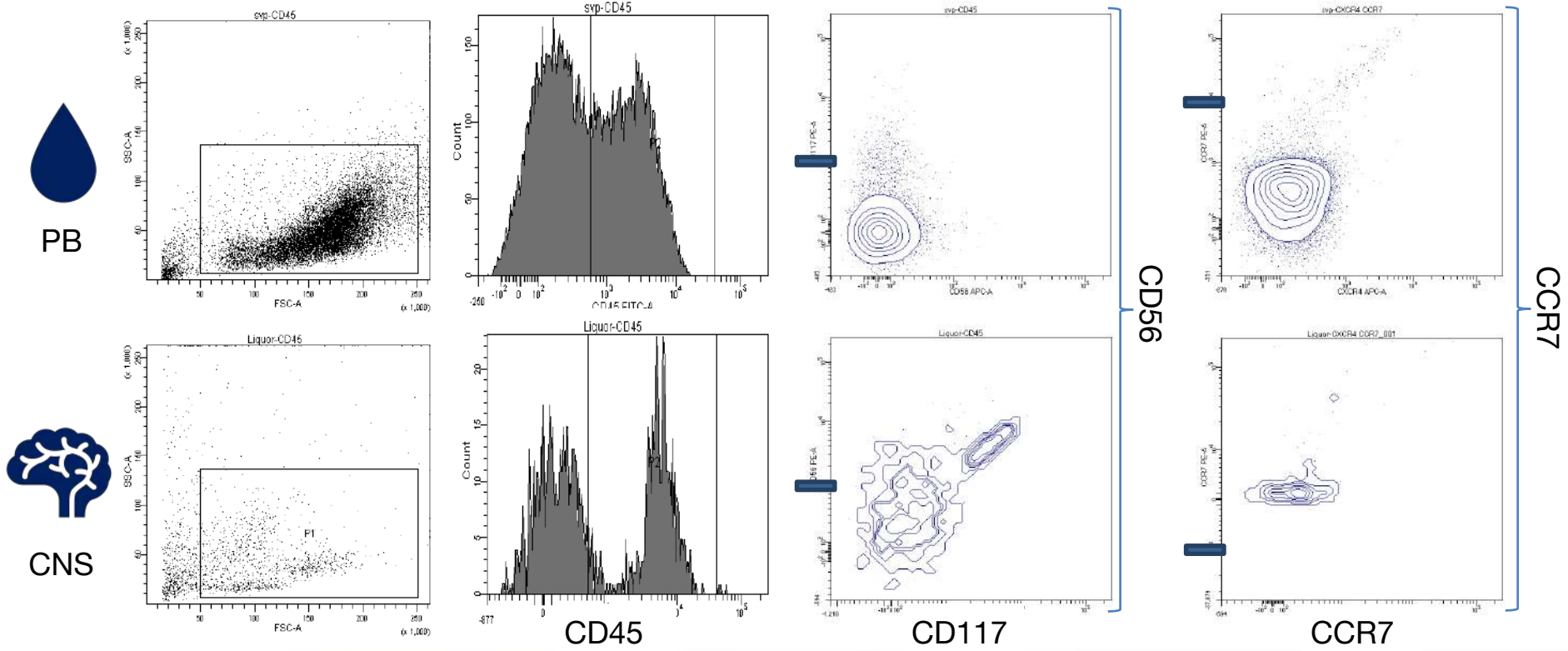


Flow cytometric analysis of blasts isolated from bone marrow, lung, and heart tissues of the same PDX

Distinctive eAML immunophenotypic signatures are stable across PDX passages



Meningeal blasts from leukemic meningitis express bright CCR7 in contrast to PB

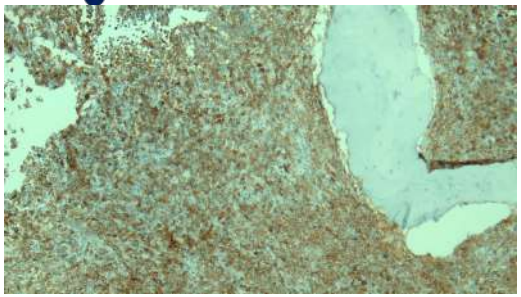


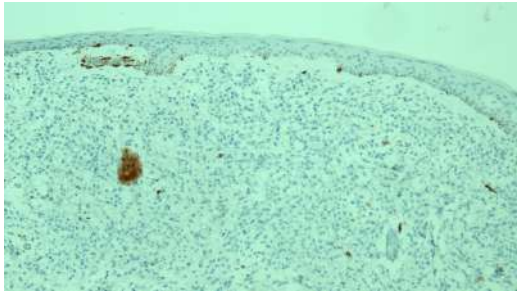
Histopathological analysis of paired BM and eAML samples confirms a distinct surface marker pattern

Bone Marrow

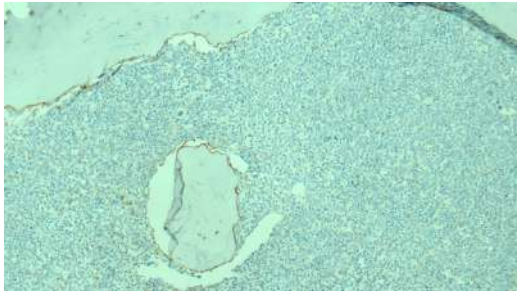
Skin

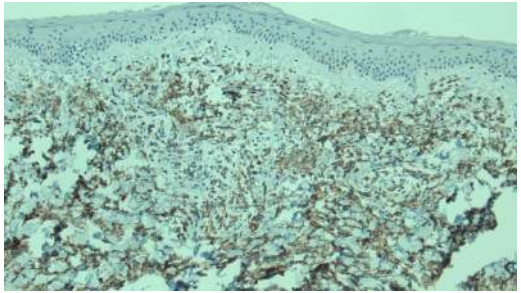
CD117



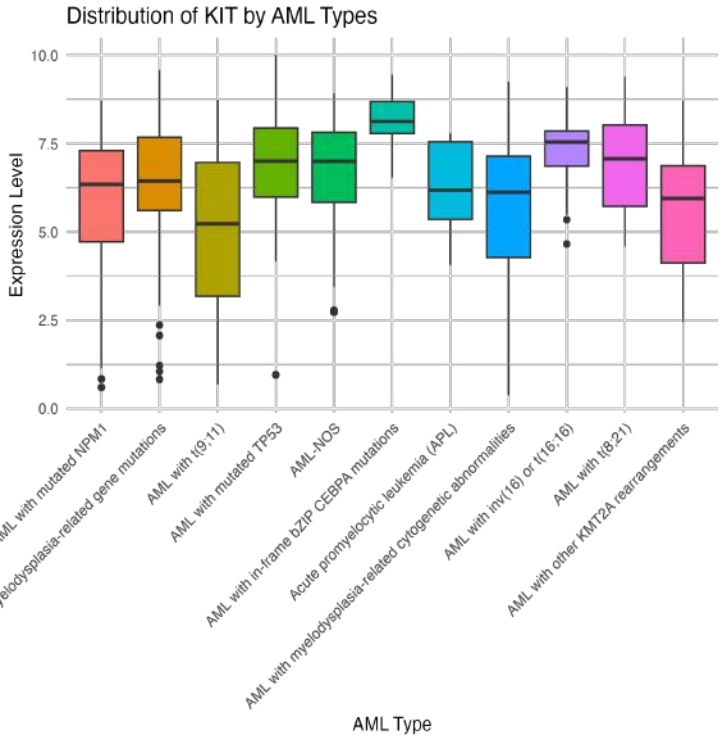


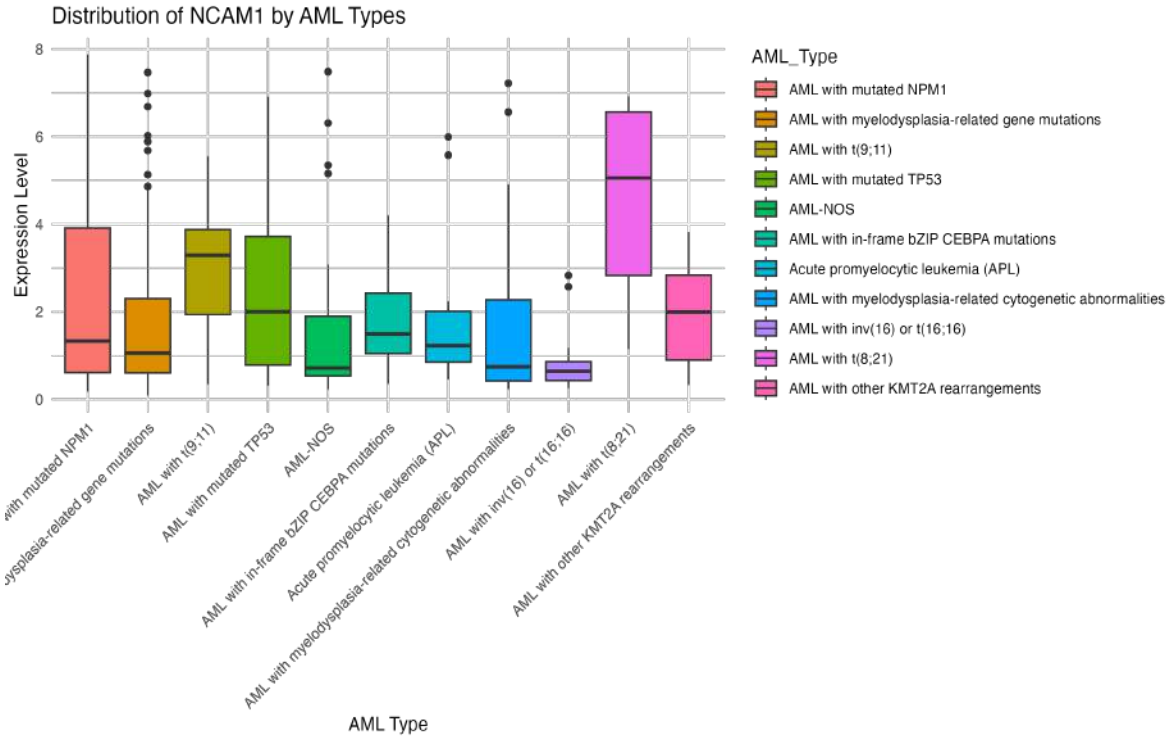
CD56





Bioinformatic analysis confirmed differentially expression of surface marker across ICC 2022 AML categories





Current limitations and future perspectives

- Lack of uniformity between PDX models and human eAML samples → new PDX models are in program.
- We are expanding the panel of surface markers under investigation, including α4β7 integrin (LPAM-1).
- Cell sorting and RNA-seq of distinct populations from extramedullary sites and leukemic masses.
- Machine learning-based interactome construction of eAML-associated proteins and pathway-centered analysis
- Suggestions and collaborative opportunities are highly welcome

University of Perugia Lab Team
- Sabrina Cipriani
- Francesca Milano
- Gaetano Cimino
- Karim Enrico Jardini
- Roberta Ranieri
- Valeria Cardinali
- Barbara Bigerna
- Alessia Tabarrini
- Chiara Caterino
- Alessandra Pucciarini

… and all the clinicians and lab collegues!

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- Ferdinando Nicoletti
- Marika Alborghetti

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- Paolo Cercola
- Daniele Remotti
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- Giuseppe Topini
- Loredana Bassi

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Director
- **Roberto Latagliata**