

Settima edizione di



AIEOP..

...in Lab

Il secretoma della nicchia leucemica favorisce l'immunosoppressione mediata da macrofagi M2 nella leucemia mieloide acuta pediatrica

Giorgia Longo

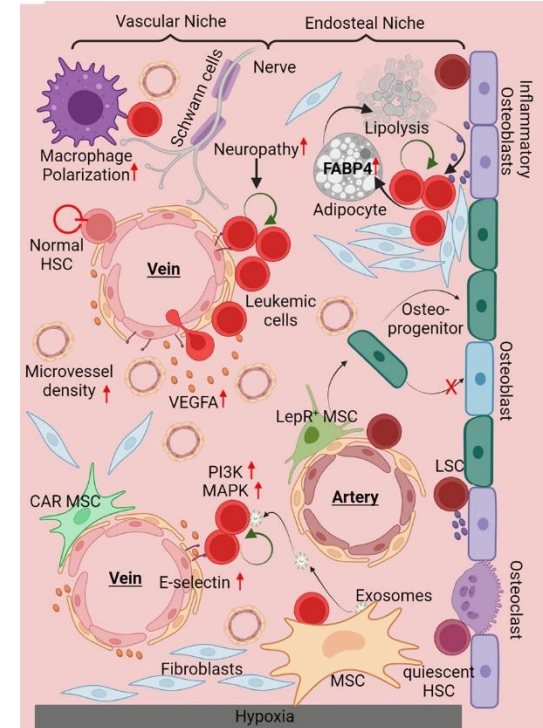
Milano, 22 e 23 maggio 2026

Disclosures of Giorgia Longo

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

AML hijacks the bone marrow niche

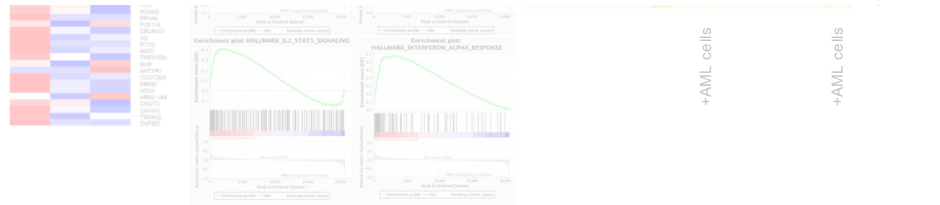
- The leukemic niche: a **complex ecosystem**
- These components form dynamic networks that:
 - Supports leukemic expansion
 - Shapes immune responses
 - Promotes therapy resistance



AML hijacks the bone marrow niche

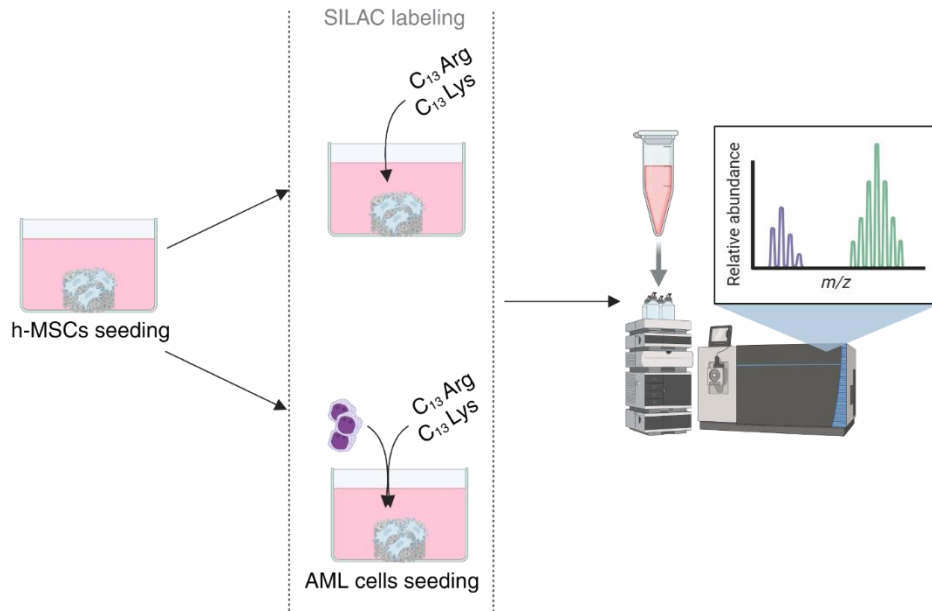


Altered-secretome signature

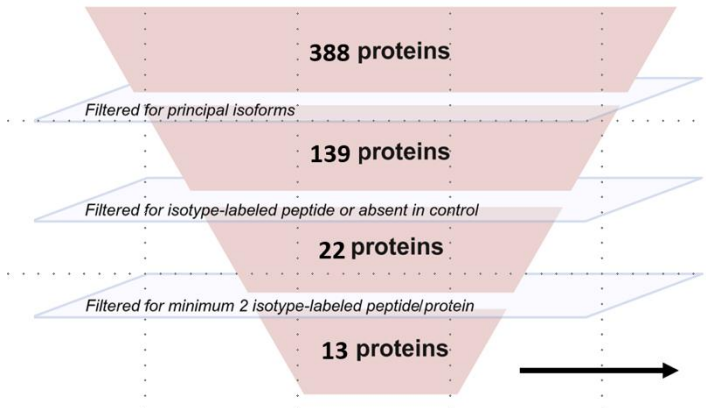
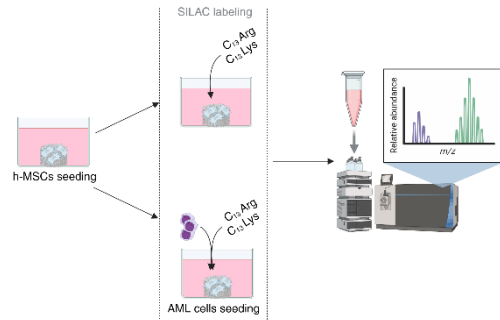


- HEALTHY MSC (h-MSC)
- AML-DERIVED MSC (AML-MSC)
- INDUCED- MSC (i-MSC, h-MSC cultured with AML blasts)

What are the changes in the secretome at leukemia onset?



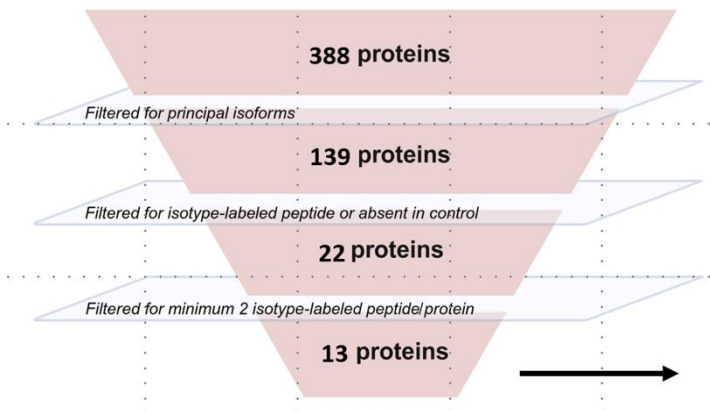
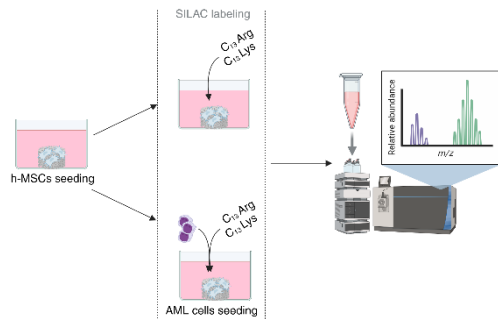
What are the changes in the secretome at leukemia onset?



PAI-1, PTX3, CHI3L1

- **SERPINE-1 (PAI-1)**: Involved in the inhibition of fibrinolysis and regulation of extracellular matrix degradation. Associated with chronic inflammation, cancer, and tissue remodeling, with pro-tumorigenic effects in various contexts.
- **PTX3 (Pentraxin 3)**: Innate immune response protein produced in response to inflammation with both protective and pro-inflammatory roles; involved in infections, tissue damage, and tumor progression.
- **CHI3L1 (YKL-40)**: Glycoprotein secreted during inflammation and linked to tumor progression, angiogenesis, and fibrosis; often elevated in cancers and inflammatory diseases.

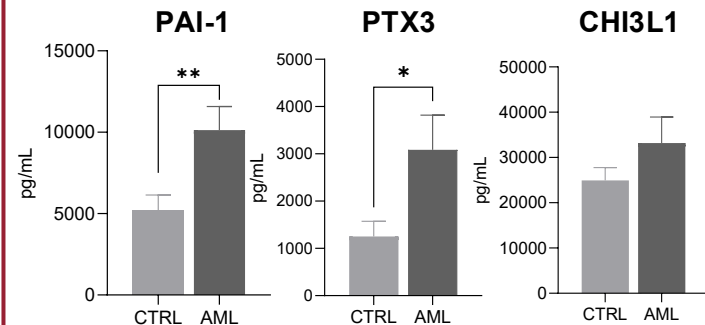
What are the changes in the secretome at leukemia onset?



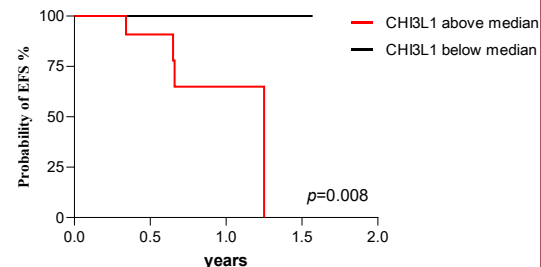
PAI-1, PTX3, CHI3L1

VALIDATION ON BM PLASMA

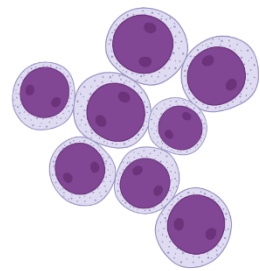
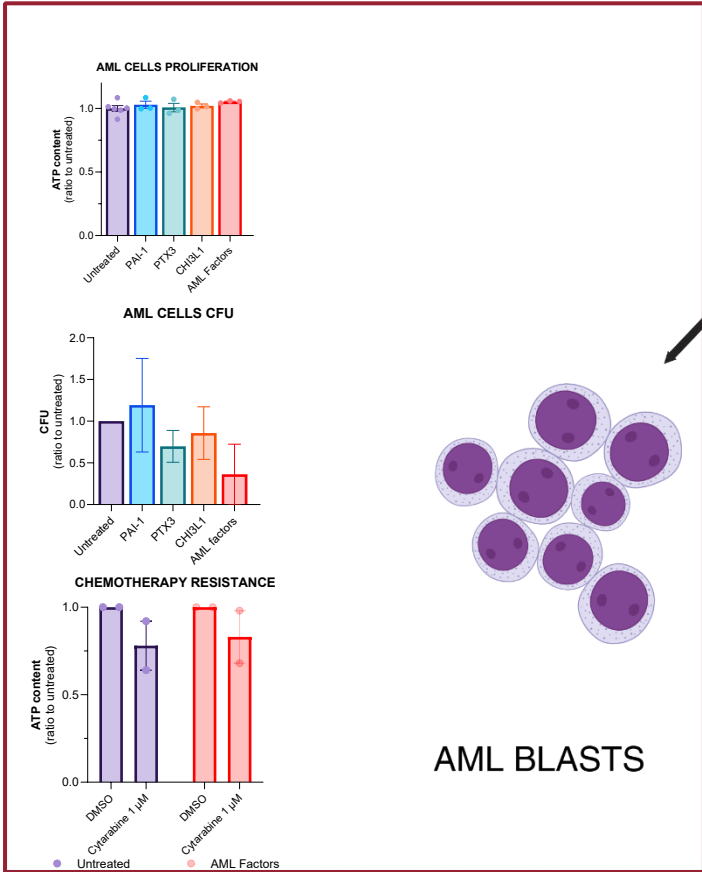
(n AML=30, ctrl n=9)



CHI3L1

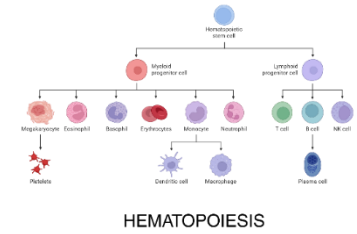
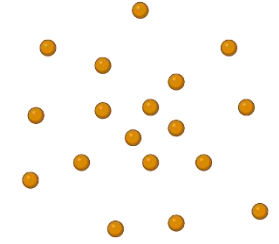


Functional effect of AML factors within the leukemic niche



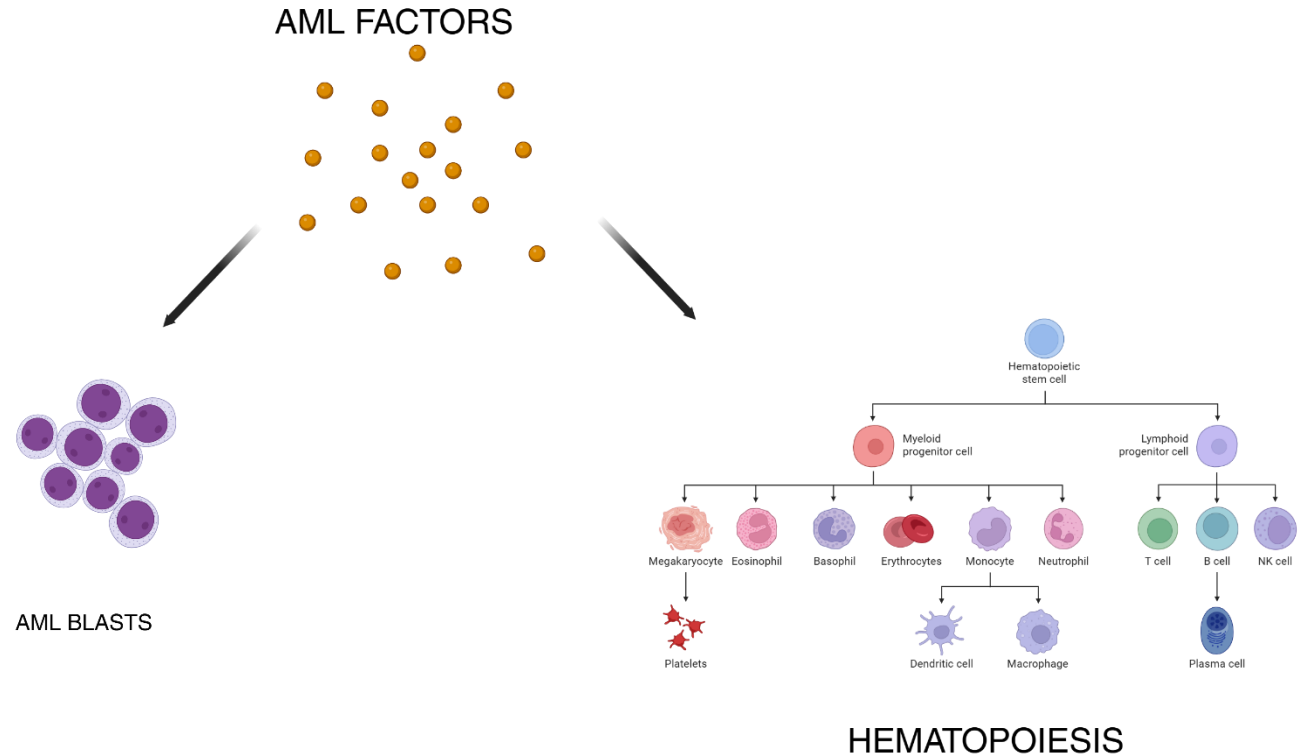
AML BLASTS

AML FACTORS

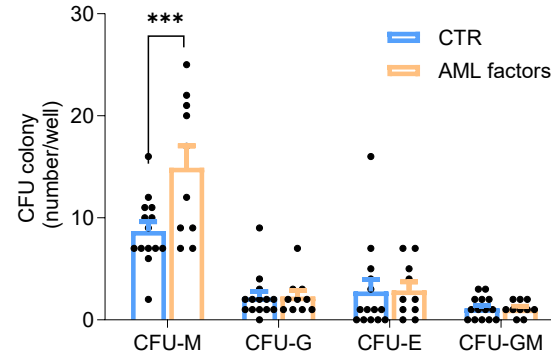
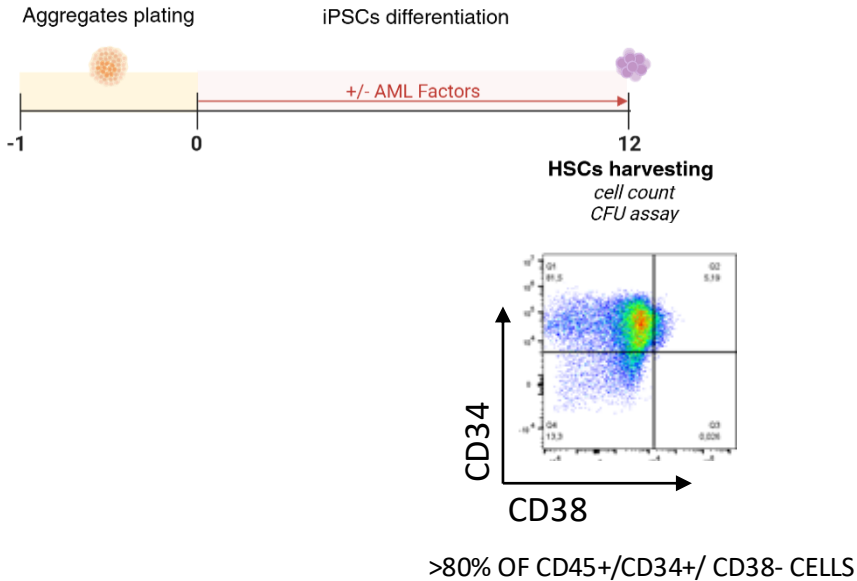


rPAI-1 + rPTX3 + rCHI3L1 = «AML FACTORS»

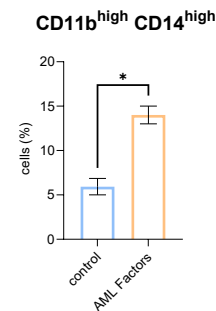
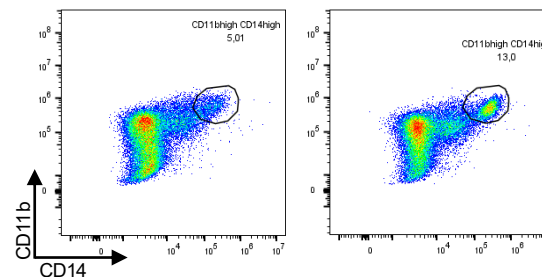
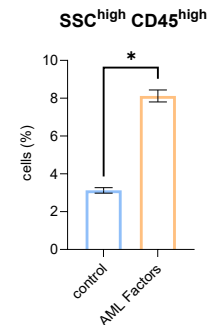
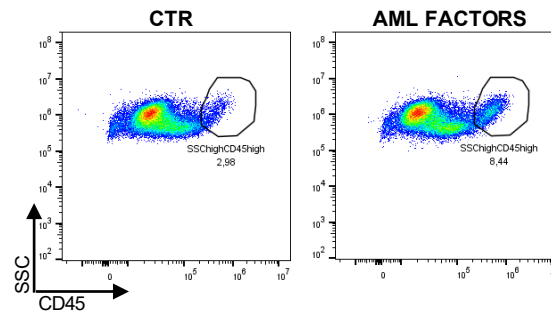
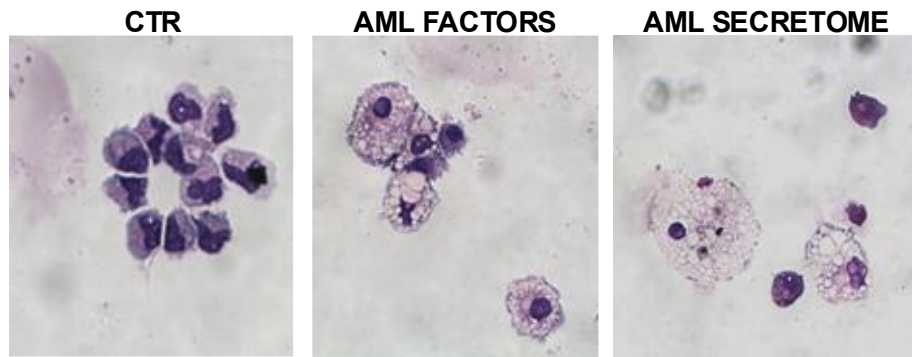
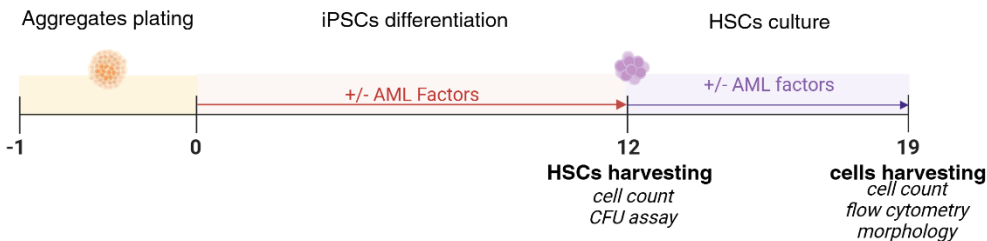
Functional effect of AML factors within the leukemic niche



AML factors shape hematopoiesis in iPSC models

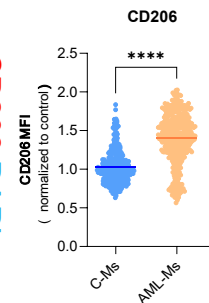
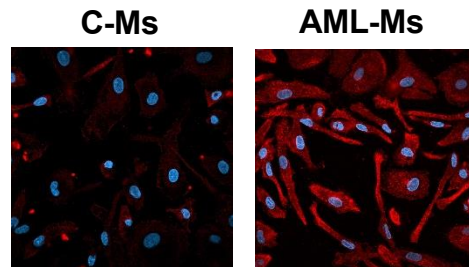
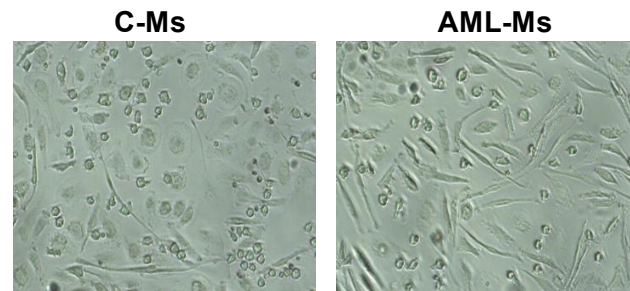
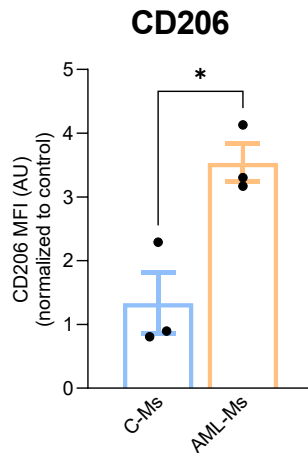
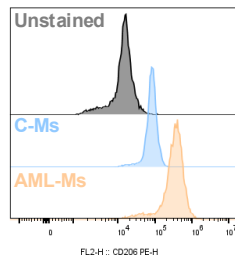
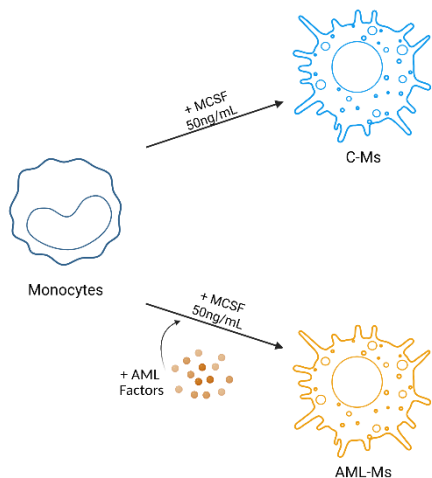


AML factors promote HSC differentiation into a monocyte /macrophage-like lineage



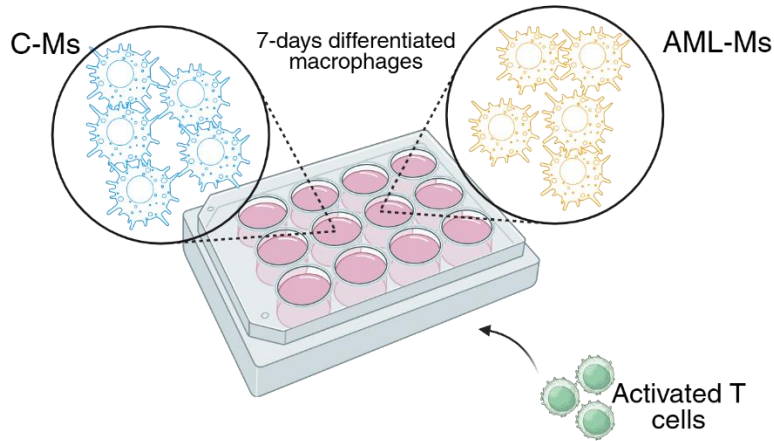
AML factors polarize macrophages toward M2-like phenotype

PBMCs-derived monocytes:

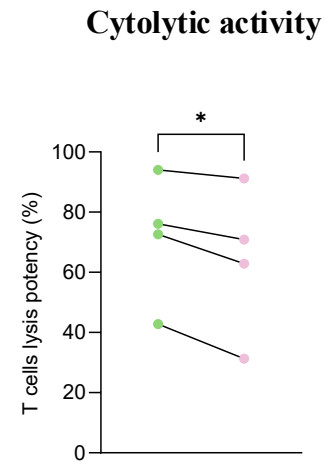
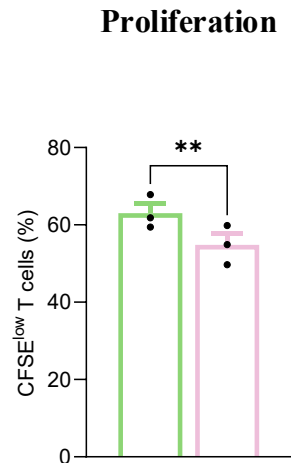
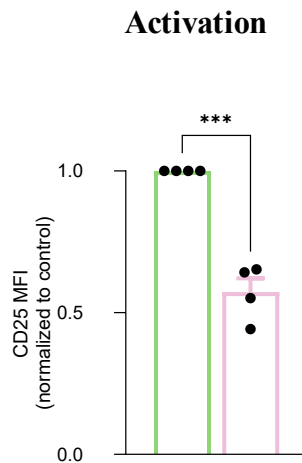
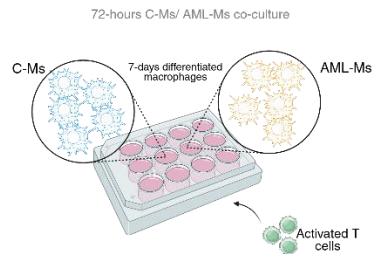


Functional effects of AML-Ms in the leukemic niche

72-hours C-Ms/ AML-Ms co-culture



Functional effects of AML-Ms in the leukemic niche

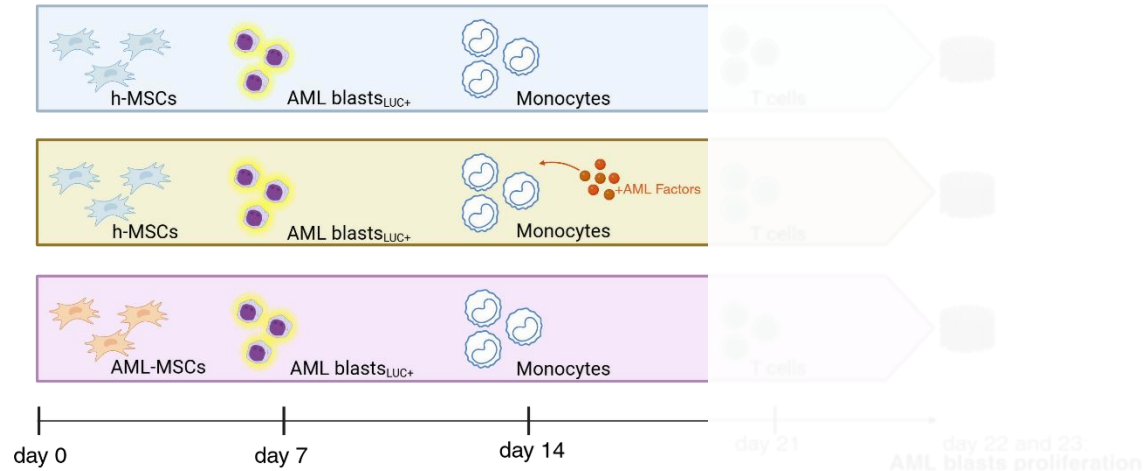


■ T cells on CTR-Ms

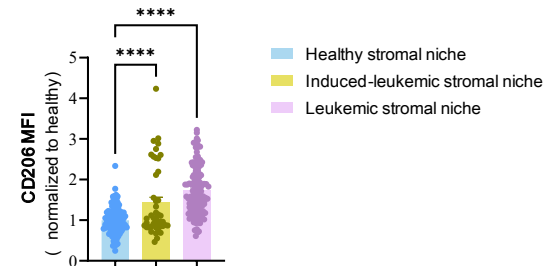
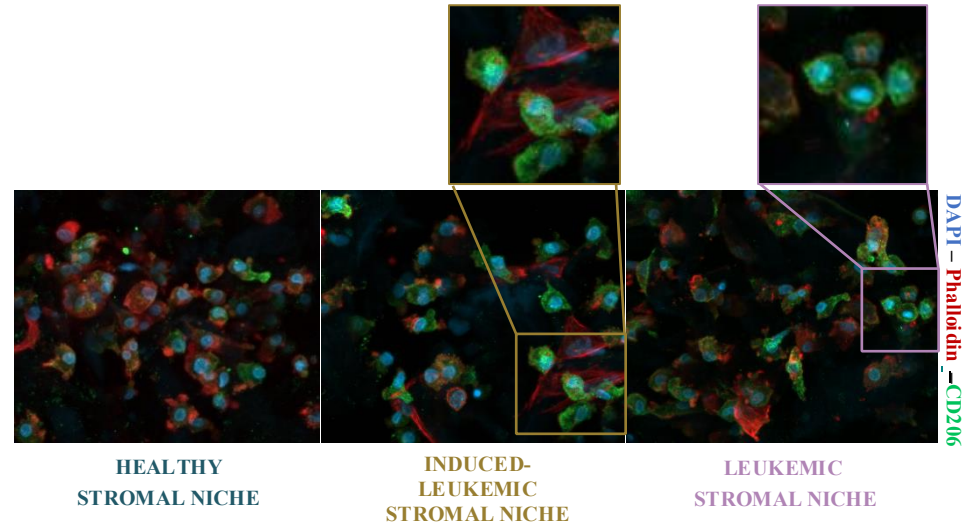
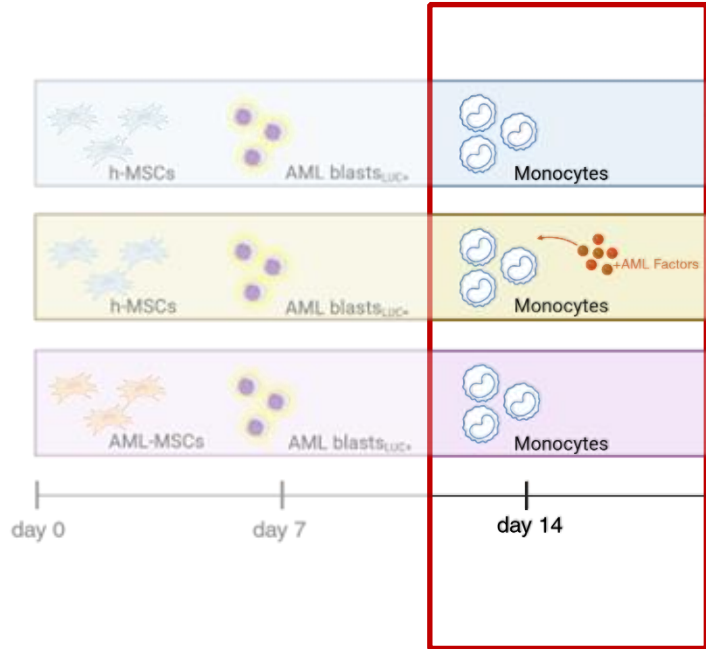
■ T cells on AML-Ms

AML-Ms exert immunosuppressive effects on T cells

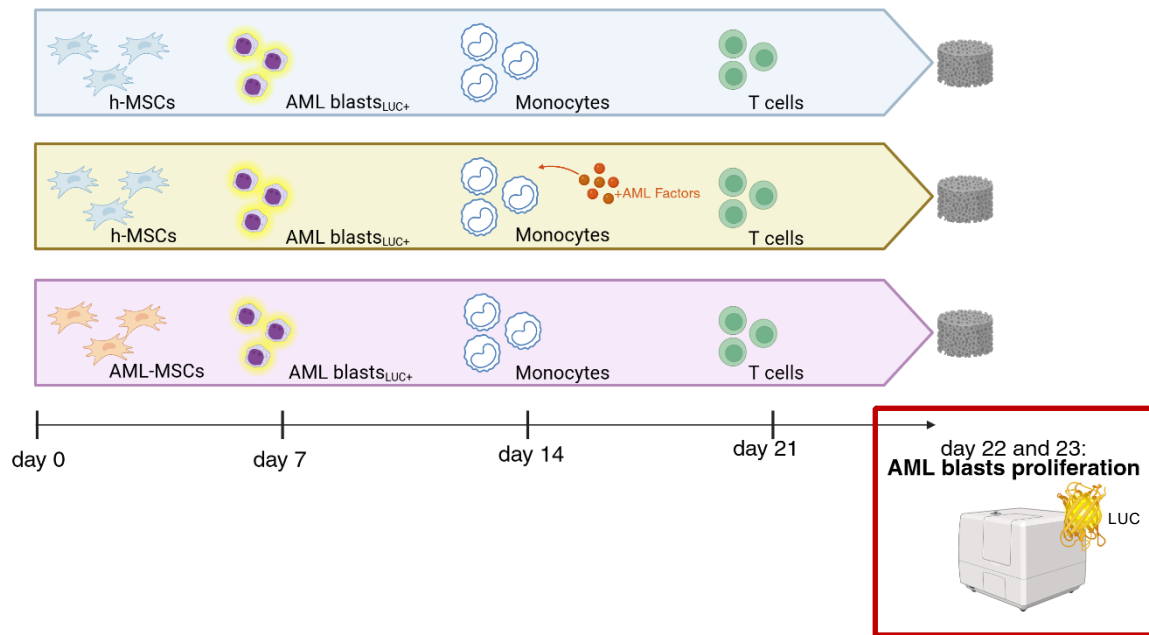
Functional effects of AML-Ms in the leukemic niche



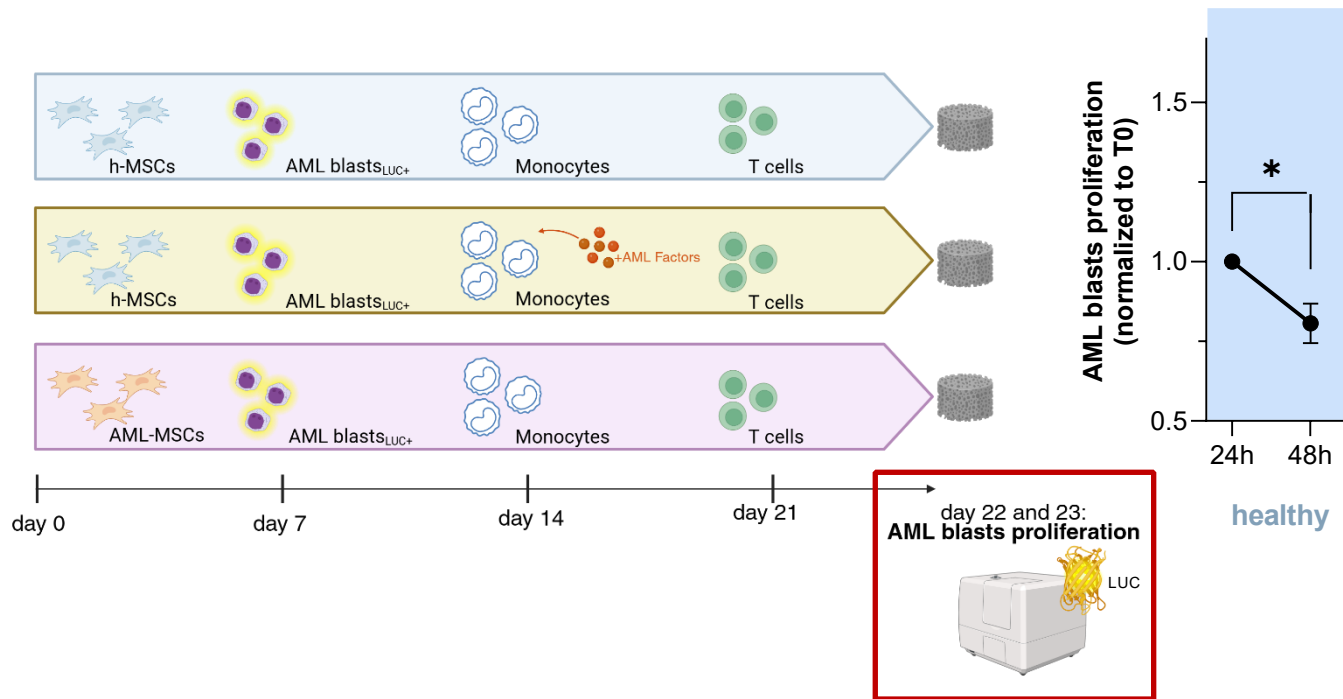
Functional effects of AML-Ms in the leukemic niche



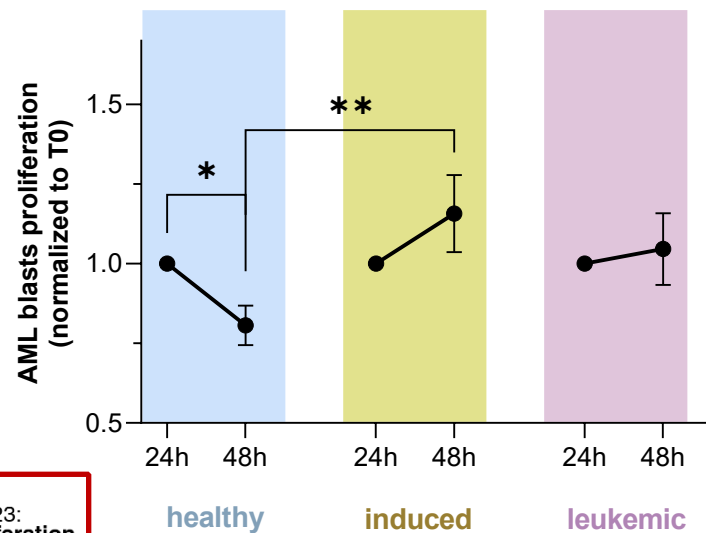
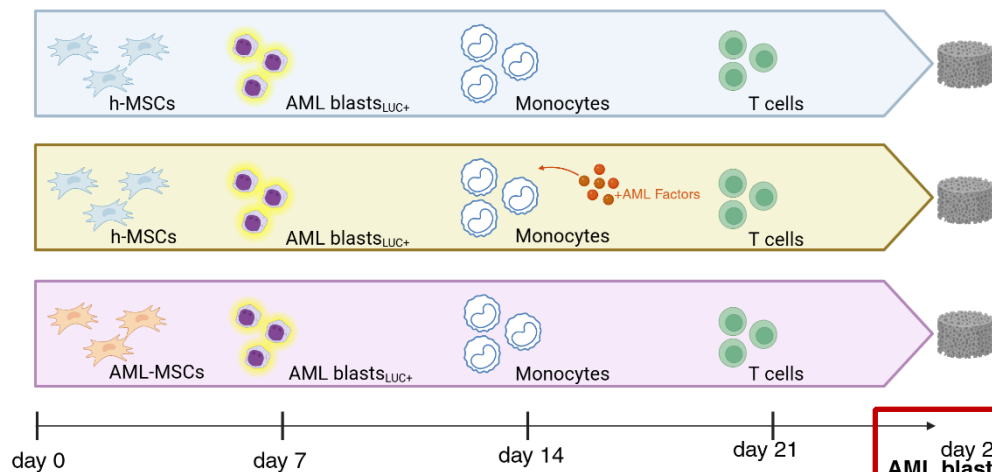
Functional effects of AML-Ms in the leukemic niche



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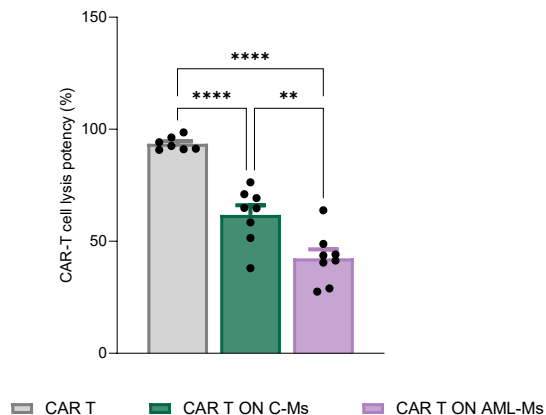
Functional effects of AML-Ms in the leukemic niche



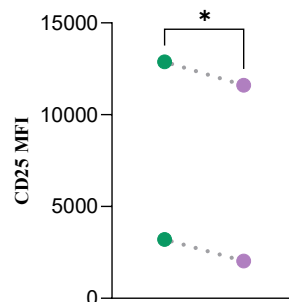
N=5

Preliminary results: AML-Ms reduce anti CD72 CAR-T cells activity

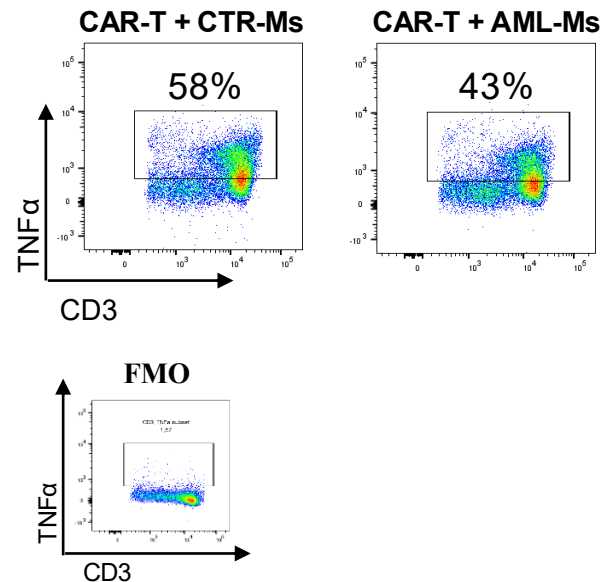
CAR T cells: Lysis potency



CAR T cells: Late activation



CAR T cells: TNF- α production



CAR-T group;

Prof. A. Biffi, Prof. M. Pigazzi,
Silvia Merlini,
Valentina Artuso,
Martina Lombi



Conclusions:

1. The AML secretome shapes **macrophage polarization** within the BM niche, with a key contribution from PAI-1, PTX3, and CHI3L1.
2. AML-educated macrophages acquire an **immunosuppressive phenotype**, leading to impaired T cell proliferation, activation, and effector function.
3. The AML secretome may represent a key determinant of patients' response to **immunotherapy** and a potential therapeutic target.



Prof. Martina Pigazzi

Dr. Claudia Tregnago
 Dr. Ambra Da Ros
 Dr. Maddalena Benetton
 Dr. Sara Perpinello
 Dr. Silvia Merlini
 Dr. Elena Barizza
 Katia Polato



**Division of Pediatric Hem-Oncology
 and Stem Cell Transplant
 DIAGNOSTIC LABORATORY (AIEOP
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**ISTITUTO DI RICERCA
 PEDIATRICA**

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