XIX CONGRESSO NAZIONALE SIES 2026

INTEGRATED MULTIOMIC IMMUNE PROFILING DEFINES THE BIOLOGICAL BASIS OF MRD PERSISTENCE IN MULTIPLE MYELOMA

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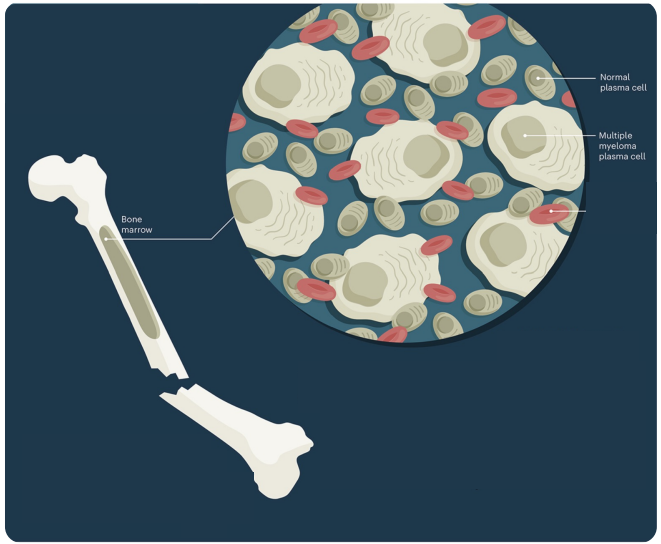
Palazzo degli Affari

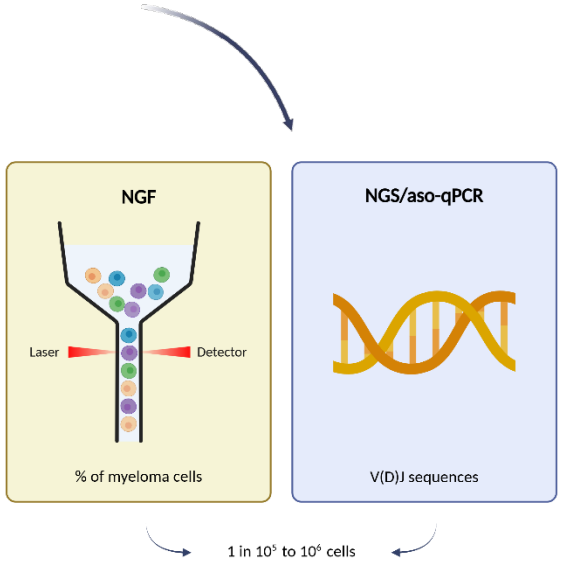
Disclosures

No disclosures to declare

Background

Minimal residual disease (MRD) measurement has emerged as an important tool for assessing response to treatment and predicting outcomes in patients with multiple myeloma.

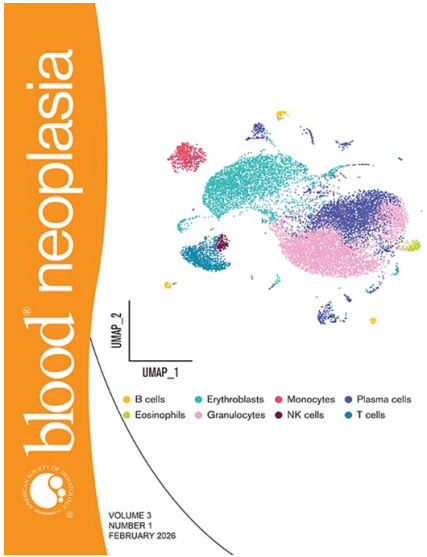




Sustained MRD has become the **new therapeutic objective** for MM treatment.

Biological rationale

The duration of the clinical response may also be driven by features of the immune microenvironment?

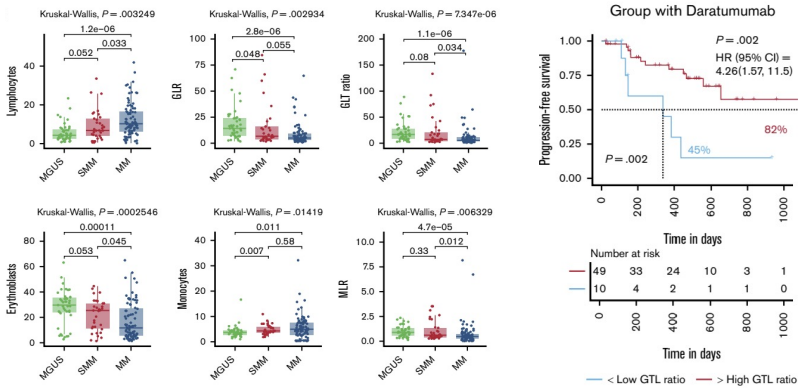


REGULAR ARTICLE

blood neoplasia

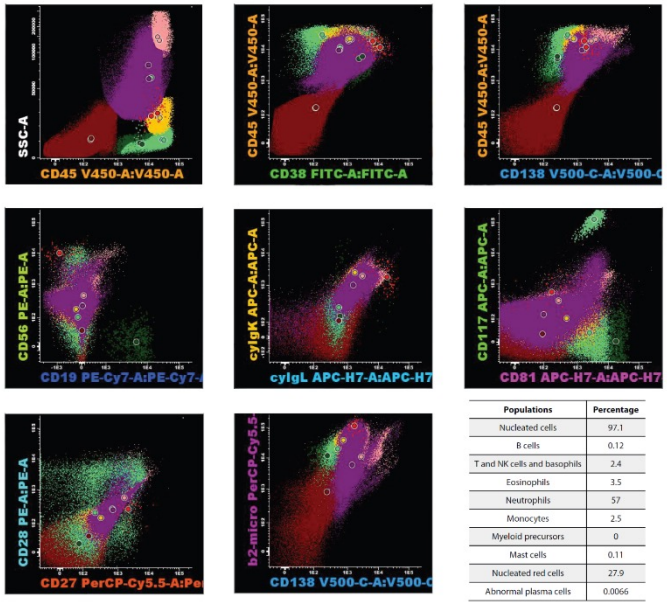
Bone marrow immune cell composition reflects multiple myeloma progression and affects treatment response

Anna Maria Corsale,[1,2] Mojtaba Shekarkar Azgomi,[1] Emilia Gigliotta,[2] Marta Di Simone,[1,2] Paola Pacelli,[3] Francesca Cioffi,[2] Elena Bestoso,[4] Donatella Raspadori,[4] Alessandro Gozzetti,[5] Antonio Solimando,[6] Paula Tabares,[6,7] Andreas Beilhack,[6,7] Maria Speciale,[2] Giusy Corsale,[2] Miriam Sciortino,[1] Cristina Aquilina,[2] Fulvio Brucato,[1] Michele Cea,[8] Renato Zambello,[9] Francesca Garofano,[2] Marta Biondo,[10] Francesca Buffa,[1,11] Nadia Caccamo,[1,11] Francesco Dieli,[1,11] Serena Meraviglia,[1,11] Sergio Siragusa,[2] and Cirino Botta[2]

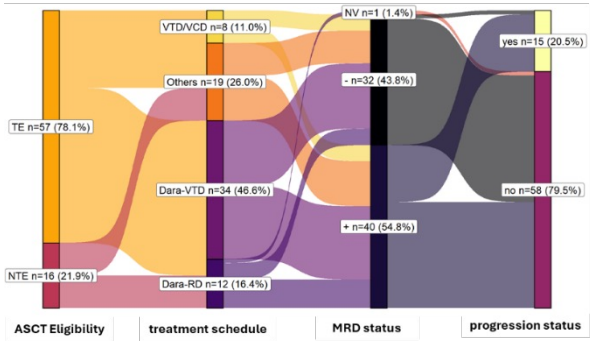


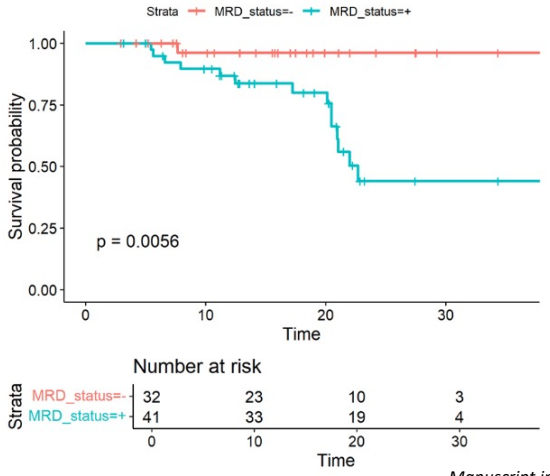
Biological rationale

Patients' characteristics		n = 74
Age		64 (36 -78)
Sex		
	F	36 (49%)
	M	38 (51%)
ISS		
	I	17 (23%)
	II	20 (27%)
	III	33 (45%)
	N/A	4 (5%)
Isotype		
	IgA/κ	6 (8%)
	IgA/λ	4 (5%)
	IgG/κ	27 (36%)
	IgG/λ	19 (26%)
	κ	10 (14%)
	λ	6 (8%)
	N/A	2 (3%)
MRD status		
	uMRD	32 (43%)
	pMRD	41 (56%)
	NE	1 (1%)



Populations	Percentage
Nucleated cells	97.1
B cells	0.12
T and NK cells and basophils	2.4
Eosinophils	3.5
Neutrophils	57
Monocytes	2.5
Myeloid precursors	0
Mast cells	0.11
Nucleated red cells	27.9
Abnormal plasma cells	0.0066





Manuscript in preparation

Methodologies

Paolo Giaccone
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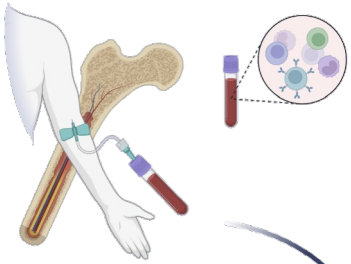
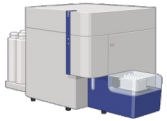
Peripheral and bone marrow blood sample collection

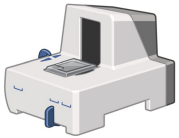


Flow cytometry and FlowCT analysis



six 10-color and two 8-color flow cytometry panels

scRNA-seq



Immunophenotypic changes in bone marrow following treatment

Undetectable MRD
(uMRD; n=14)

Persistent MRD
(pMRD; n=9)

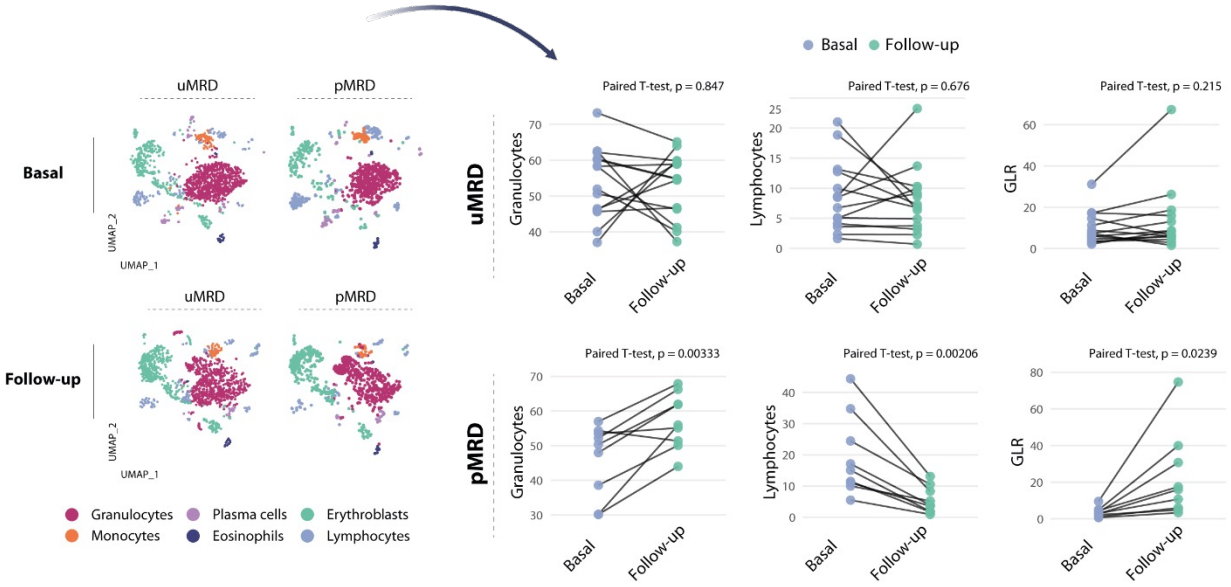
six 10-color and two 8-color flow cytometry panels

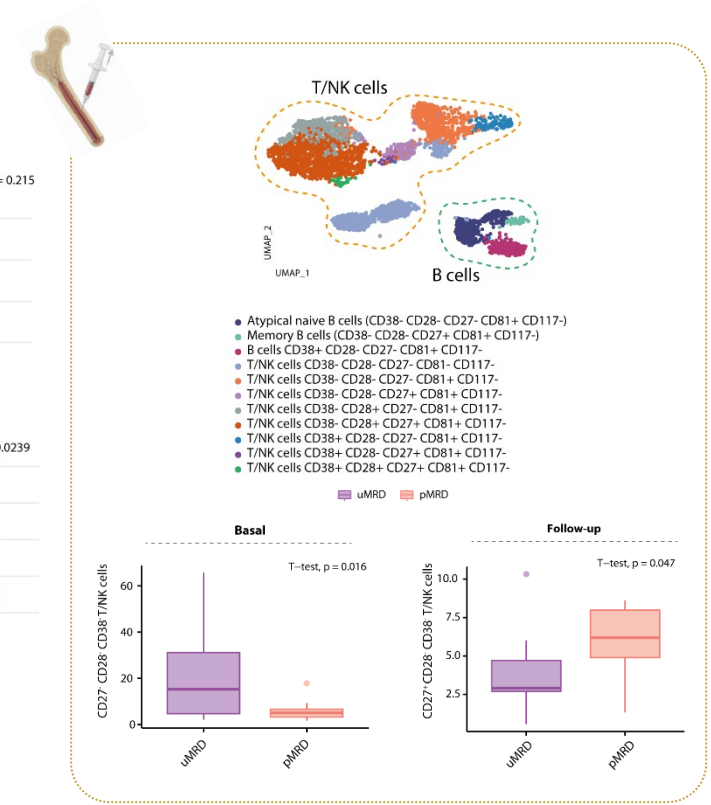
	FITC	PE	PerCP-Cy5.5	PE-Cy7	APC	APC-H7	V450[a]	V500-C[a]
PCST	CD38	CD56	β2-microglobulin	CD19	cyIgκ[b]	cyIgλ	CD45	CD138
PCD	CD38	CD28	CD27	CD19	CD117	CD81	CD45	CD138

a. BD Horizon™ V450, BD Horizon™ V500-C
b. cy refers to cytoplasmic

Characteristic	Undetectable MRD	Persistent MRD
Number of patients	n= 14 (61%)	n= 9 (39%)
Therapy		
Dara + RD	1 (7%)	1 (11%)
Dara + VTD	12 (86%)	6 (67%)
VTD	1 (7%)	2 (22%)

Immunophenotypic changes in bone marrow following treatment

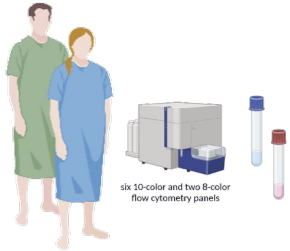


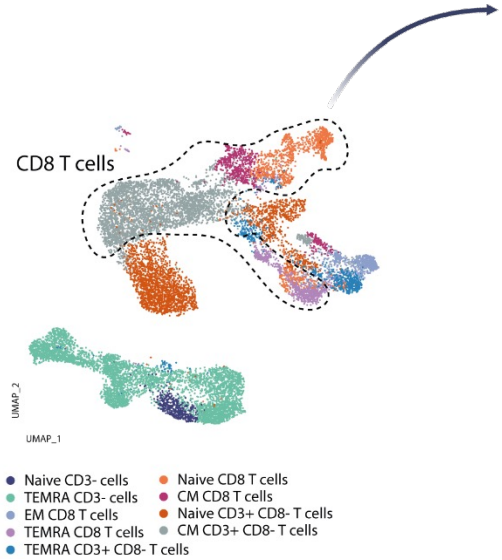


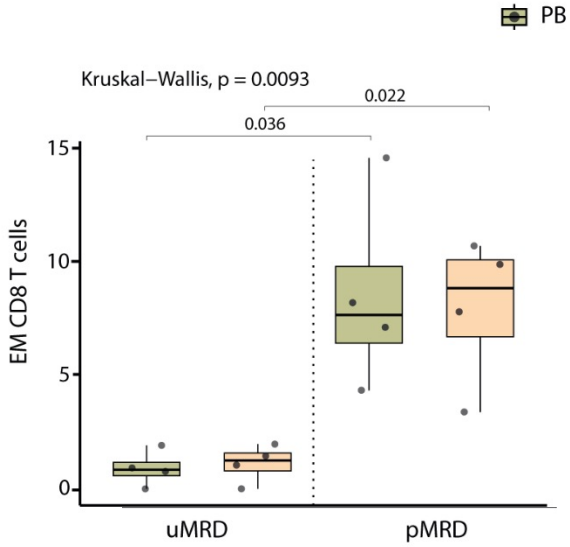
Differential distribution of CD8 T cell subsets in uMRD and pMRD patients

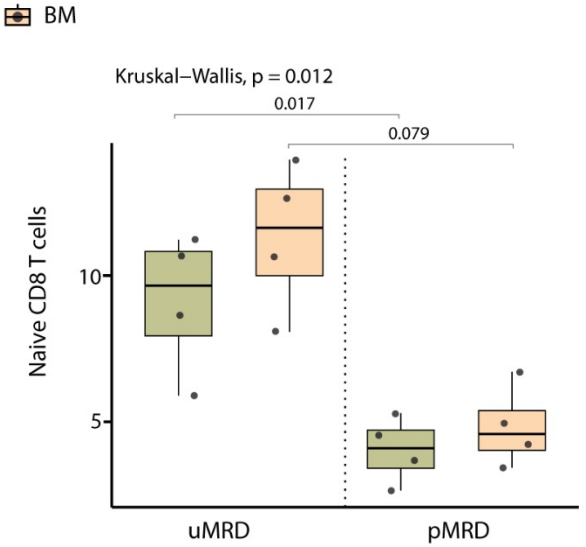
Undetectable MRD
(uMRD; n=4)

Persistent MRD
(pMRD; n=4)





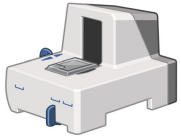




Transcriptional profiles distinctly separate pMRD and uMRD

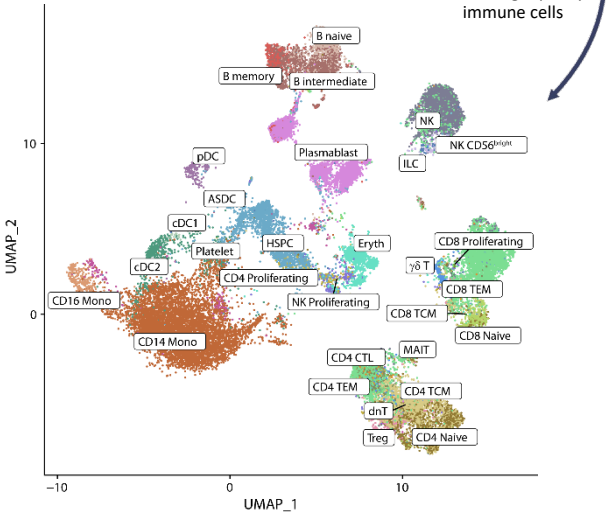
Undetectable MRD
(uMRD; n=4)

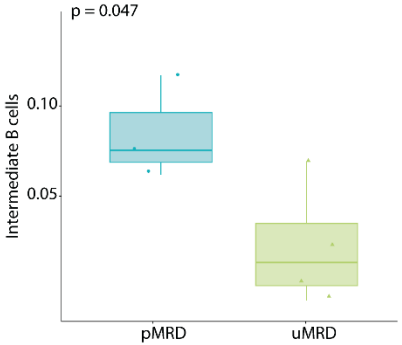
Persistent MRD
(pMRD; n=3)

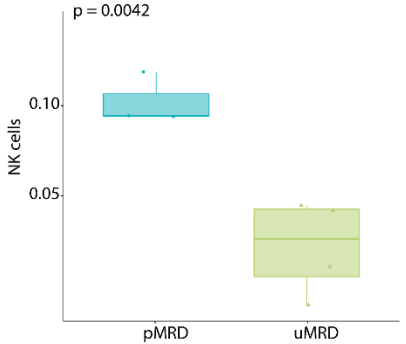


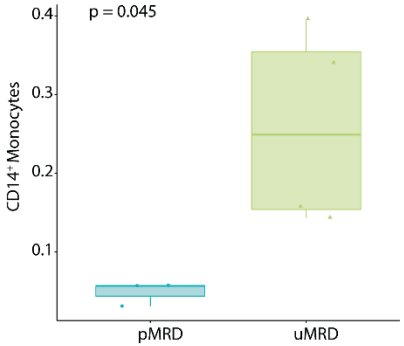
scRNA-seq

36,383 high quality immune cells



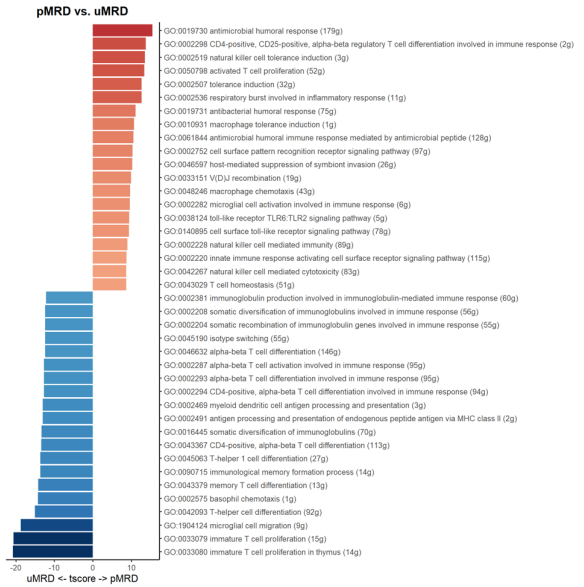


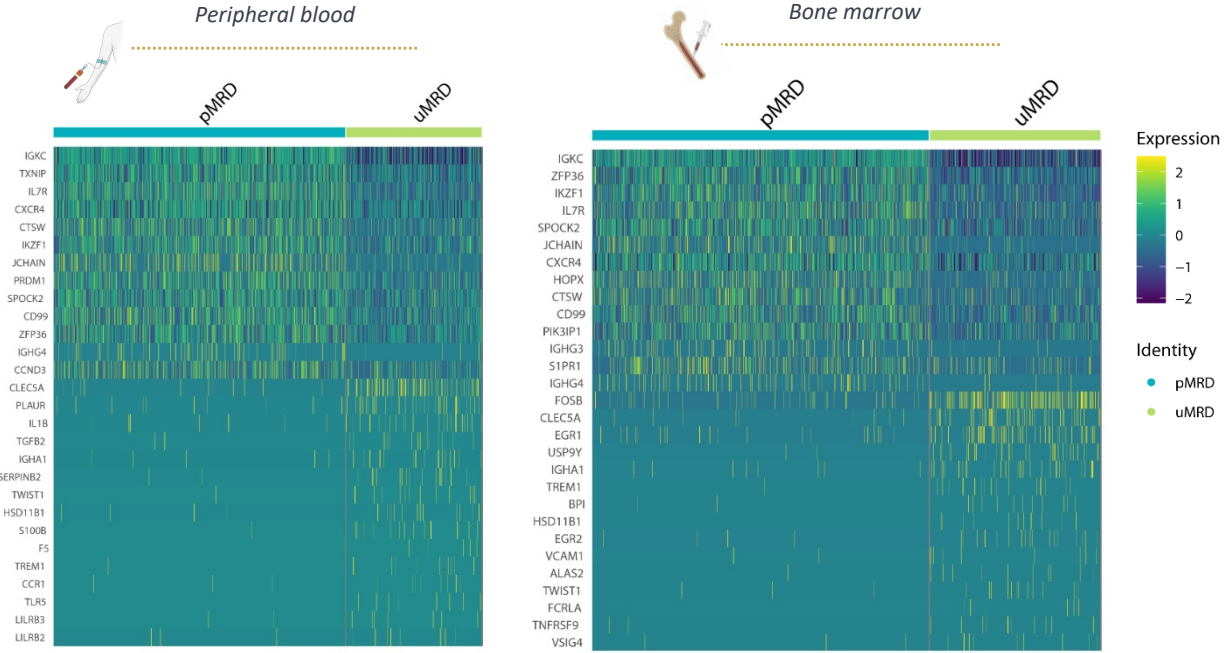




Transcriptional profiles distinctly separate pMRD and uMRD

CD8 EM

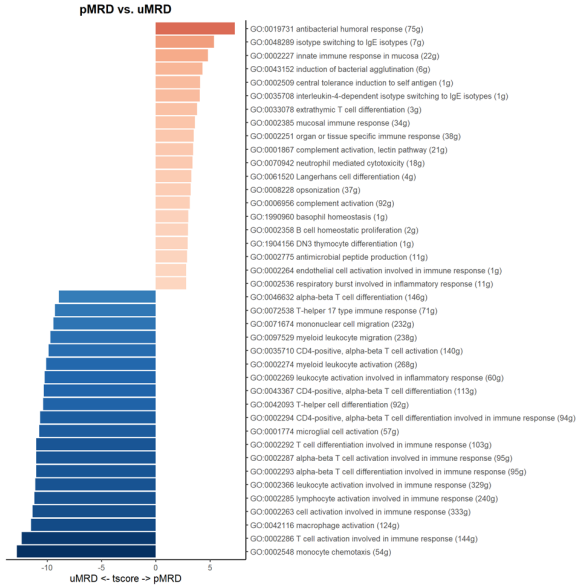


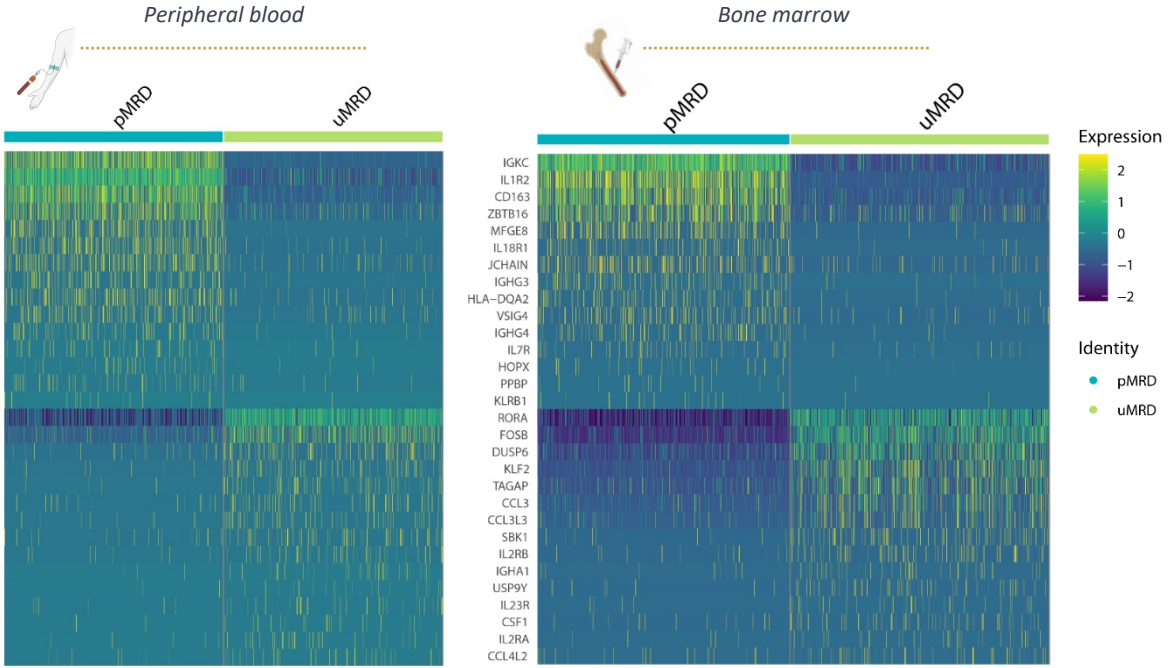


uMRD patients display enrichment of adaptive and memory-related CD8⁺ programs, consistent with effective tumor control.
pMRD patients show signatures of chronic activation and reduced functional diversity.

Transcriptional profiles distinctly separate pMRD and uMRD

CD14^{+} Monocytes





uMRD monocytes display pro-inflammatory and T-cell–supportive programs.
pMRD monocytes adopt a regulatory, innate-skewed phenotype.

Take home messages

Our findings reveal two distinct immune trajectories following therapy:

MRD eradication

is marked by balanced lympho–myeloid proportions, preservation of naive T-cell pools, and inflammatory myeloid cell reprogramming.

MRD persistence

is characterized by reduced immune diversity, and plasma cell–imprinted transcriptional states across immune subsets.

Persistent MRD is not simply a tumor-intrinsic phenomenon, but reflects a resistant, tumor-influenced immune ecosystem.

Acknowledgements

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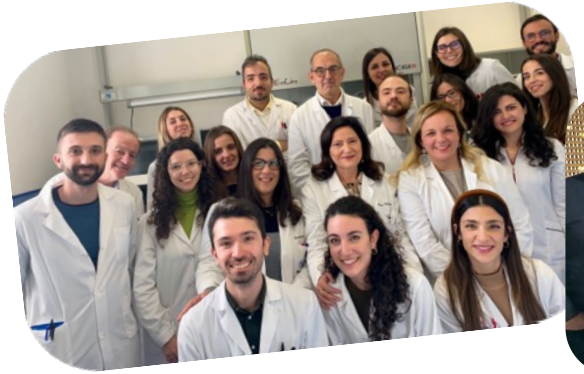

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All patients