BCR-ABL1 And *JAK2* V617F Mutations In Mesoangiogenic Progenitor Cells Suggest A Common Bone Marrow Precursor For Hematopoietic And Stromal Cell Niche

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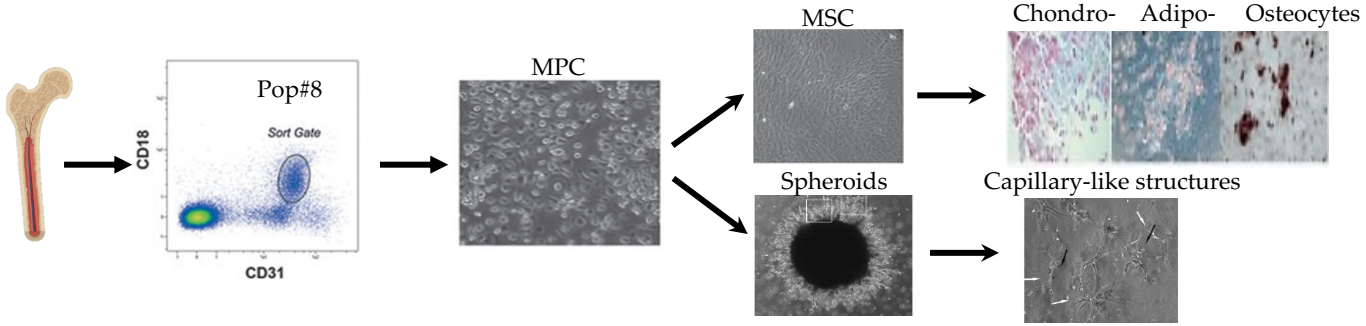
Disclosures of Irene Sofia Burzi

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

No conflict of interest to disclose

Background: Mesangiogenic Progenitor Cells (MPCs) and Pop#8



Pop#8 Surface Markers
CD64bright CD31bright CD14- CD18+
Lin- CD34- CD38+ CD13dim CD33+
CD11b,c- CD14- CD15- CD16- CD44+ CD45dim HLA-DR+
CD309- CD144- CD133-
CD105- MSCA1- STRO1- CD146-

MPCs Surface Markers
CD18+ CD31+ CD73- CD90-
CD166, CD115, CD116, CD36, CD44, CD13, CD11a,b,c, CD45, HLA-DR

Considering Pop#8 and MPCs immunophenotype, we suppose the existence of a shared progenitor with monocytes

Petrini M. *et al*. Stem Cells and Development 2009; Pacini *et al*. Stem Cells And Development, 2016; Pacini S. *et al*. Oncotarget 2019

Hypotesis

- Hematopoietic and stromal stem cells of the bone marrow could share a common progenitor
- Currently, the relationship between the hematopoietic and the stromal niche is still debated
- Myeloproliferative disorders (*BCR-ABL1* and *JAK2* V617F) are neoplasms of the hematopoietic stem cells
- To evaluate a common stem cell progenitor for myeloid and stromal bone marrow stem cells we isolated MPC from patients with myeloproliferative disorders and assessed the presence of *BCR-ABL1* and *JAK2* V617F

Experimental Design

Hematological patients

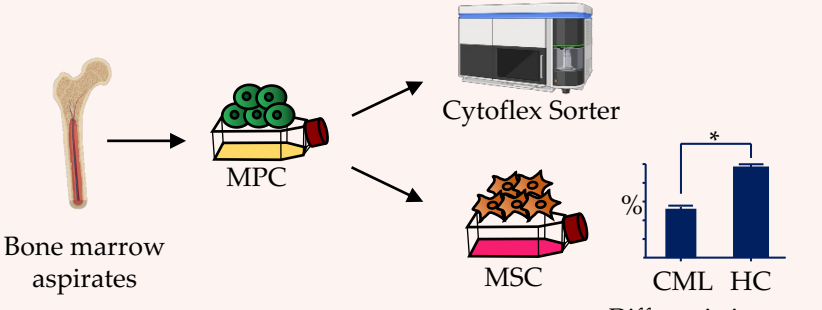
CML patients

n=15

MPN patients

n=3

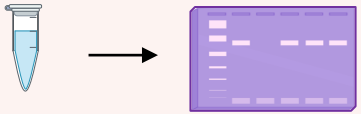
MPC isolation, purification and differentiation



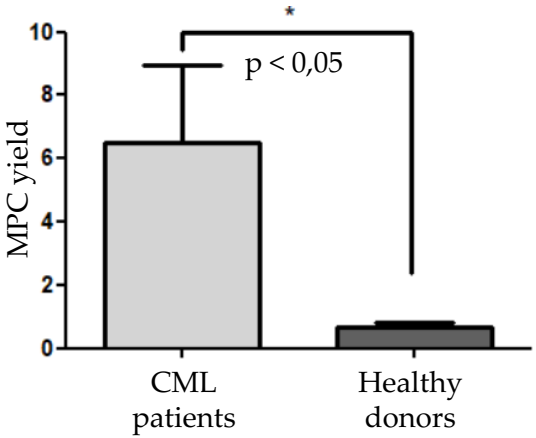
Tumor-associated mutations detection

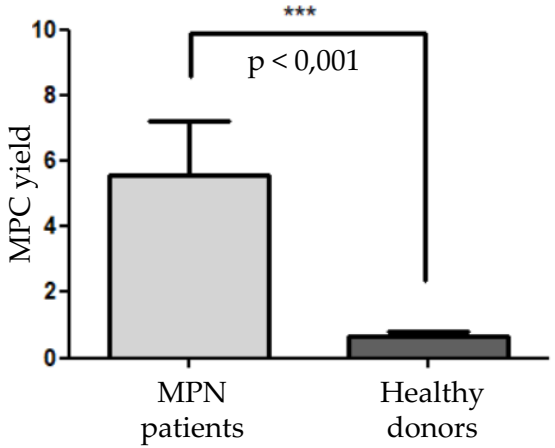
CML *BCR-ABL1* samples

MPN *JAK2* V617F samples



Results: MPC isolation and yield





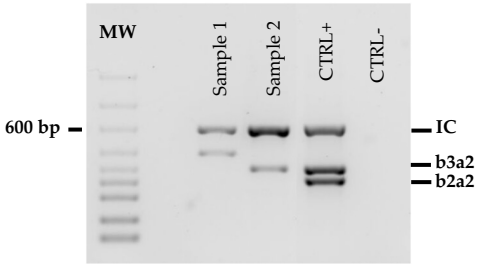
CML samples	
MPC yield	6,21%

Healthy Donors	
MPC yield	0,68%

MPN samples	
MPC yield	5,61%

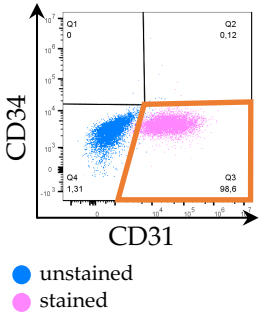
Results: *BCR-ABL1* mRNA detection in MPC and MSC isolated from CML bone marrow

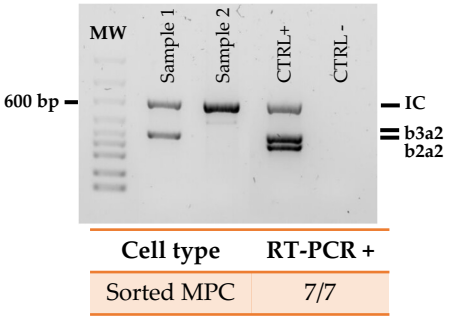
BCR-ABL1 mRNA in non sorted MPC



Cell type	RT-PCR +
Non sorted MPC	6/8

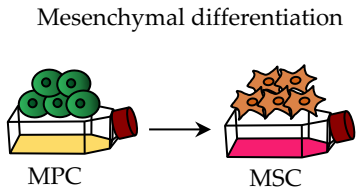
BCR-ABL1 mRNA in FACS-sorted MPC

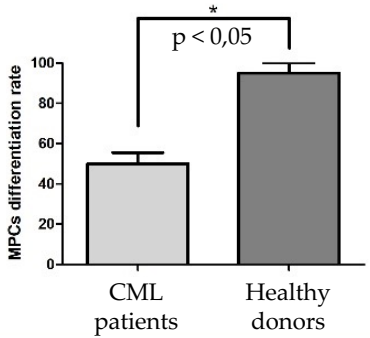


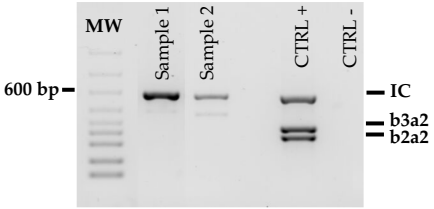


Cell type	RT-PCR +
Sorted MPC	7/7

MPC differentiation and *BCR-ABL1* mRNA in MSC



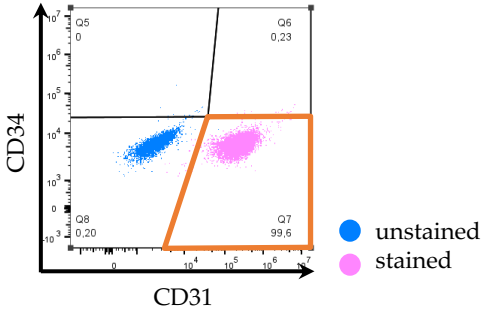


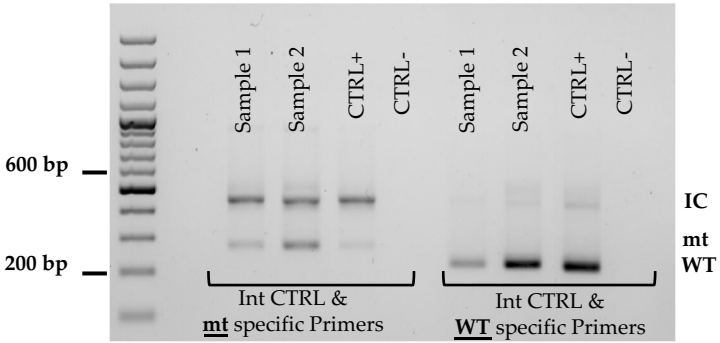


Cell type	RT-PCR +
MPC-derived MSC	3/4

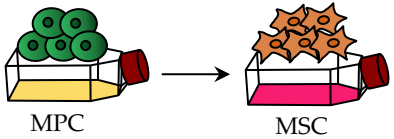
Results: *JAK2* V617F detection in MPC and MSC isolated from MPN bone

JAK2 V617F in FACS-sorted MPC





Mesenchymal differentiation



Cell type	ARMS-PCR +
Sorted MPC	3/3
MPC-derived MSC	1/1

Conclusions

- The culture yield of MPCs in patients with CML and MPN is significantly higher than that of healthy donors
- The mesengenic differentiation is compromised in MPC derived from bone marrow of patients affected by CML Ph+
- *BCR-ABL1* mRNA and *JAK2* V617F allele is detectable in MPCs and MPC-derived MSC
- Our data support the hypothesis that MPCs can derive from a hematopoietic precursor

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Thank you for your attention!

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