4295 ESTABLISHING DISTINCT CYTOKINE SIGNATURES DIFFERENTIATING BETWEEN ACUTE MYELOID LEUKEMIA, MYELODYSPLASTIC SYNDROME AND CHIP USING BONE MARROW RNA OR CELL-FREE RNA (cfRNA)

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INTRODUCTION

Cytokines are essential for various immune functions and the overall inflammatory response to myeloid neoplasms in bone marrow. They play a major role in bone marrow microenvironment in normal and abnormal hematopoiesis. Cytokines exert their functions by interacting with their receptors and full evaluation of cytokines role requires evaluating their receptors as well. Using next generation sequencing (NGS) and machine learning, we measured the expression of 36 cytokines/chemokines and cytokines receptors in the bone marrow (BM) of patients with acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), and clonal hematopoiesis of indeterminate potential (CHIP)..

AIM

We explored if RNA levels as evaluated using NGS can establish a specif cytokines signatures that differentiate between AML, MDS, CHIP and normal in bone marrow and if the same model can also distinguish between these diseases if peripheral blood cell-free RNA (cfRNA) reflects BM environment.

METHOD

RNA was extracted from the bone marrow (BM) samples of patients with AML (N=515), MDS (825), and CHIP (N=915). cfRNA was extracted from the peripheral blood of patients with AML (N=30), MDS (N=184), and CHIP (N=502). BM RNA and cfRNA were sequenced using 1500 gene targeted RNA next generation sequencing (NGS) panel. The expression levels of 36 cytokine/chemokines were used in this analysis. Random forest algorithms were developed using Two-thirds of the BM samples and top-ranked biomarkers to build signatures that distinguish between two diagnostic classes. One-third of the bone marrow samples were used for testing these algorithms. Each model was then used to test if cfRNA samples show the same results obtained from BM samples.

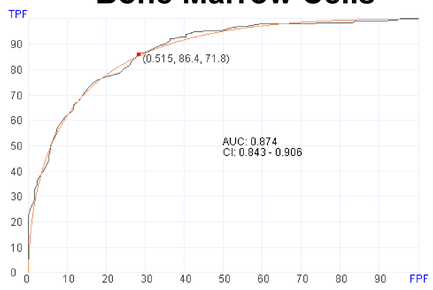
RESULTS

MDS Vs AML

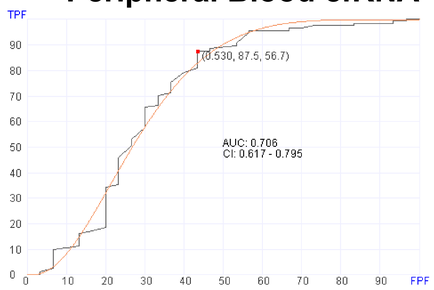
	MDS (TPM)	AML (TPM)	Log P-Value
TGFBI	4.50	3.45	-Infinity
TNFRSF10D	2.93	3.59	-Infinity
TNFRSF4	3.20	3.69	-Infinity
TGFBR3	3.72	3.18	-15.95
IL2	2.10	1.63	-13.85
TNFRSF10B	4.28	4.59	-11.87
IFNG	4.27	3.58	-11.56
CXCL8(IL8)	8.13	7.50	-10.06
IL7R	5.47	4.67	-9.60
CTLA4	2.82	2.46	-7.90
TNF	4.96	4.59	-7.82
TNFAIP3	7.38	7.03	-7.16
IL1RAP	3.66	4.16	-5.60
CXXC4	2.29	1.68	-5.50
IL3RA	3.52	3.93	-5.32
TGFBR2	5.50	5.41	-2.27
TNFRSF14	5.23	5.14	-2.04
IL12RB2	1.71	1.84	-1.61
CXCR4	5.51	5.84	-1.28
IL21R	2.24	2.19	-0.68

20 cytokines in Bone marrow cellular RNA and peripheral blood cfRNA can distinguish between MDS Vs AML :

Bone Marrow Cells



Peripheral Blood cfRNA

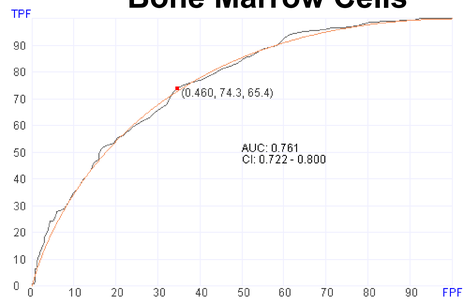


MDS Vs CHIP

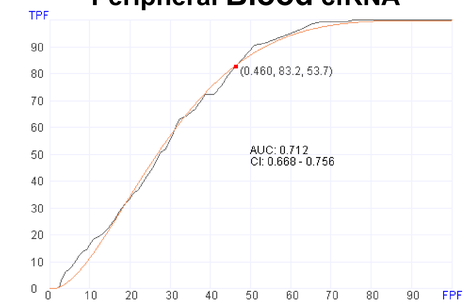
	MDS (TPM)	CHIP (TPM	Log P-Value
TGFBR2	5.50	5.78	-Infinity
IL1RAP	3.66	4.23	-11.50
IL1B	4.25	4.67	-11.13
TNFRSF14	5.23	5.46	-10.80
TNFRSF9	2.36	2.59	-8.80
TNFAIP3	7.38	7.74	-8.12
IL21R	2.24	2.51	-7.38
CTLA4	2.82	3.10	-6.78
TNF	4.96	5.22	-5.84
CXCR4	5.51	6.31	-5.50
IL3	1.59	1.25	-4.02
TNFRSF4	3.20	3.34	-3.04
IL12RB2	1.71	1.86	-2.92
CXCL8(IL8)	8.13	8.39	-2.73
TGFBR3	3.72	3.87	-2.73
TNFRSF10D	2.93	3.01	-2.22
IL13RA2	0.98	0.85	-2.16
TNFRSF10B	4.28	4.36	-2.04
TNFRSF17	1.58	1.66	-1.14
IL7R	5.47	5.49	-0.36

20 cytokines in Bone marrow cellular RNA and peripheral blood cfRNA can distinguish between MDS Vs CHIP :

Bone Marrow Cells



Peripheral Blood cfRNA



CONCLUSIONS

-Signatures of cytokines/chemokines and their receptors in bone marrow environment are disease-specific and can distinguish between AML, MDS and CHIP.

-Peripheral blood cfRNA reflects bone marrow environment and can be used as an alternative to bone marrow in monitoring cytokines/chemokines and their receptors.

CONTACT INFORMATION

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