3316 ESTABLISHING A DISTINCT CYTOKINE SIGNATURE FOR MULTIPLE MYELOMA USING BONE MARROW RNA AND PERIPHERAL BLOOD CELL-FREE RNA (CFRNA)

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INTRODUCTION

The combined effects of cytokines/chemokines and their receptors are believed to play a major role in determining the overall environment for plasma cell growth and the clinical course of multiple myeloma (MM). Cytokines also play significant role in the immune response to the neoplastic plasma cells and are relevant to various therapeutic approaches. Numerous studies evaluated various cytokines individually and correlated with clinical behavior. We explored the potential of establishing cytokine receptors signatures.

AIM

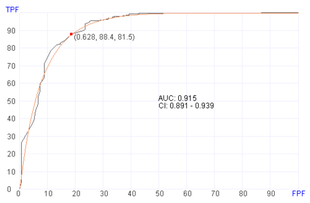
We used next generation sequencing (NGS) and RNA quantification along with machine learning algorithms to establish signatures based on the levels of cytokine/chemokine and their receptors that distinguish MM from other lymphoid neoplasms.

METHOD

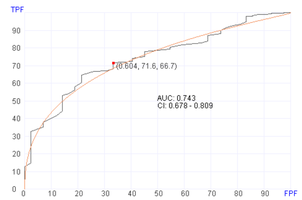
RNA was extracted from the bone marrow samples of patients with MM (N=409), chronic lymphocytic leukemia (CLL) (184), and bone marrow samples without any molecular evidence of abnormalities (N=430). RNA was also extracted from lymph nodes with diffuse large B-cell lymphoma (DLBCL)(N=287). cfRNA was extracted from cfRNA from the peripheral blood of 430 normal individuals, 23 patients with MM, 19 patients with DLBCL, and 16 patients with CLL. Tissue RNA and cfRNA were sequenced using 1600 gene targeted RNA next generation sequencing (NGS) panel. Only 36 cytokines/chemokines and their receptors are used in generating the models using Bayesian algorithm and random forest. After establishing these models in tissue, we tested them using cfRNA.

RESULTS

Tissue RNA



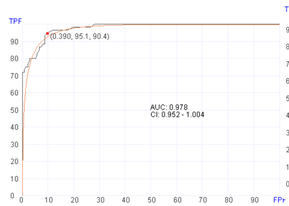
Peripheral Blood cfRNA



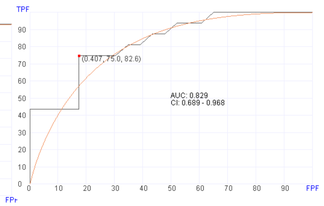
10 markers MM Vs Normal

Bone marrow	MM (TPM)	Normal (TPM)	Log P-Value
ACACA	3.10	3.85	-Infinity
CXCR4	4.75	6.77	-Infinity
IL12RB2	1.35	1.96	-Infinity
IL1RAP	2.53	4.40	-Infinity
TGFBR2	4.49	5.85	-Infinity
TGFBR3	2.73	3.85	-Infinity
TNFAIP3	6.19	7.77	-Infinity
TNFRSF10B	3.43	4.36	-Infinity
TNFRSF10D	2.36	3.08	-Infinity
TNFRSF14	4.44	5.52	-Infinity
TNFRSF17	3.87	1.76	-Infinity

Tissue RNA



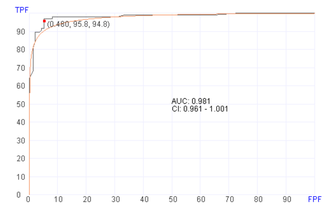
Peripheral Blood cfRNA



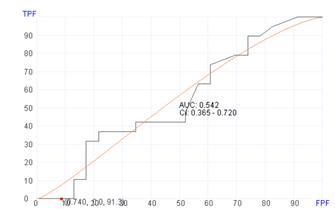
10 markers MM Vs CLL

Bone marrow	MM (TPM)	CLL (TPM)	Log P-Value
CTLA4	2.08	4.75	-Infinity
IL21R	1.69	3.61	-Infinity
TGFBI	3.99	5.21	-Infinity
TGFBR2	4.49	6.29	-Infinity
TGFBR3	2.73	4.33	-Infinity
TNFRSF10B	3.43	5.03	-Infinity
TNFRSF10D	2.36	3.29	-Infinity
TNFRSF14	4.44	5.73	-Infinity
TNFRSF9	1.65	2.77	-Infinity
CXXC4	2.67	3.10	-1.45

Tissue RNA



Peripheral Blood cfRNA



10 markers MM Vs DLBCL

Bone marrow/Lymph o node	MM (TPM)	DLBCL (TPM)	Log P-Value
CTLA4	2.08	3.75	-Infinity
IL21R	1.69	4.65	-Infinity
IL2RA	1.10	3.12	-Infinity
TGFB3	1.71	3.42	-Infinity
TGFBR2	4.49	5.62	-Infinity
TNFRSF10B	3.43	4.82	-Infinity
TNFRSF4	2.68	4.47	-Infinity
TNFRSF6B	2.57	4.28	-Infinity
TNFRSF9	1.65	3.75	-Infinity
TNFAIP3	6.19	6.04	-1.17

CONCLUSIONS

- Bone marrow microenvironment in multiple myeloma is unique and distinct from other lymphoid neoplasms.
- MM cytokine signature is driven mainly by TNF pathway.
- Peripheral blood cfRNA, in general, reflects bone marrow MM cytokine signature.

CONTACT INFORMATION

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