Expression of CD229 on Bone Marrow Cellular Compartment and its Relevance in Multiple Myeloma

Sandeep Rai PhD, Ritu Gupta MD, Nupur Das MD
Department of Laboratory Oncology, All India Institute of Medical Sciences, New Delhi, India



Background

CD229 has been claimed to be a useful plasma cell (PC) gating marker in MM using Multiparameter flow cytometry (MFC), however, studies are sparse and limited to a small cohort of patient samples enrolled in clinical trials.

Objective

This study analyses the expression profile of CD229 on PC and its ability to delineate normal from aberrant PC (NPC vs APC). CD229-based PC gating was also evaluated with that of traditionally used markers (CD138 & CD38).

Materials & Methods

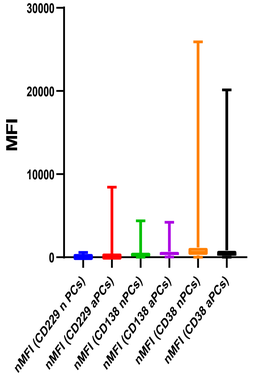
Prospective analysis of patients diagnosed with MM (per standard IMWG criteria) in Tertiary care cancer center. A total of 78 patients with a diagnosis of MM (29 treatment naïve & 59 on therapy). Bone marrow aspirates from patients diagnosed with MM were collected in EDTA and processed for MFC using a single tube 14-color antibody panel was used which consisted of cy-kappa FITC, cy-lambda PE, CD45 Texas-red, CD19 PE-Cy5.5, CD56 PE-Cy7, CD117 APC, CD38 APC700, CD81 APC-H7, CD138 BV421, CD27 BV510, CD3 BV605, CD20 BV650, CD28 BV711, CD229 BV786.

Main Outcomes Measures: 1. Differential expression of CD229 on NPC & APC 2. Comparison of CD229-based PC gating with CD138 and CD38

Result

Expression of CD138, CD38, and CD229 was evaluated on PC, hematogones (HGs) and non-PCs. The expression of CD229 was homogenous on both PC and HG compartments as compared to CD38 and CD138. On comparing the expression patterns, it was found to be statistically significant between PC, HG, and non-PC for all three markers ($p<0.001$). aPC showed under-expression of CD38 and overexpression of and CD138 and CD229 as compared to nPC and was found to be statistically significant for CD138 and CD38 (CD138, p=<0.0001; CD38, p=0.0020) over CD229 (p=0.1134).

Expression profile of CD138, CD38 and CD229 on nPC vs aPC



Expression of CD229, CD138 and CD38 on plasma cells (PC), hematogones (HG) and non-PC

Type of cases	nMFI of CD229; Median (range)			p-value	
	PC	HG	Non-PC	PC vs HG	PC vs non-PC
All MM (n=78)	50.64 (6.64 – 347.48)	18.49 (1.42 – 57.82)	1.95 (1.08 – 26.81)	<0.0001	<0.0001
NDMM (n=29)	50.28 (11.71 – 347.48)	18.21 (2.39 – 57.82)	2.17 (1.13 – 9.66)	0.215	0.1752
MM on Rx (n=49)	53.48 (6.64 – 178.14)	18.78 (1.42 – 48.82)	1.89 (1.08 – 26.89)	<0.0001	<0.0001
	nMFI of CD138; Median (range)				
All MM (n=78)	335.76 (57.19 – 4299.17)	1.99 (1.09 – 69.64)	2.00 (1.14 – 75.65)	<0.0001	<0.0001
NDMM (n=29)	287.41 (71.69 – 1238.45)	2.03 (1.09 – 69.64)	2.17 (1.16 – 4.42)	<0.0001	<0.0001
MM on Rx (n=49)	374.10 (57.19 – 4299.27)	1.96 (1.30 – 26.92)	1.93 (1.14 – 75.65)	<0.0001	<0.0001
	nMFI of CD38; Median (range)				
All MM (n=78)	492.17 (7.13 – 24820.11)	102.96 (1.50 – 5037.06)	7.65 (1.04 – 183.39)	0.0015	0.0014
NDMM (n=29)	1061.96 (19.32 – 16988.75)	123.14 (4.16 – 2570.30)	8.90 (1.61 – 181.98)	<0.0001	<0.0001
MM on Rx (n=49)	321.17 (7.13 – 24820.11)	81.52 (1.50 – 5037.06)	6.75 (1.04 – 183.39)	<0.0001	<0.0001

Conclusion

This study shows that CD229 can be used for the identification of PCs and due to relatively homogenous expression; it can be used as a suitable marker for targeted therapies. However, CD229 is not a satisfactory marker for discriminating NPC from APC, thus limiting its ability as a useful marker of diagnostic relevance and residual disease assessment in MM case

Discussion

Flow cytometric immunophenotyping of PC has proven to be of utility in the diagnosis, classification, prognostic stratification, and monitoring of MRD in PCPD patients. Accurate identification of PC and their clear-cut discrimination from other bone marrow cells is a critical step in this process. At present, combined assessment of CD138 and CD38, together with CD45, FSC, and SSC, is considered the standard approach for the identification and gating of PC compartments. However, in recent years new therapeutic antibodies against a variety of molecules expressed on the surface of PC, including CD38 and CD138, have been developed and are currently under evaluation for the treatment of MM patients.

References

1. Van de Donk, Niels W C J et al. Multiple myeloma. The Lancet, Volume 397, Issue 10272, 410 – 427. DOI: https://doi.org/10.1016/S0140-6736(21)00135-5
2. Boccadoro, Mario. Multiple Myeloma and Related Disorders. The Lancet Oncology, Volume 5, Issue 12, 765. DOI:https://doi.org/10.1016/S1470-2045(04)01657-2
3. Ritu Gupta, MD, DNB, Archana Bhaskar, MSc, Lalit Kumar, MD, Atul Sharma, DM, Paresh Jain, MD, Flow Cytometric Immunophenotyping and Minimal Residual Disease Analysis in Multiple Myeloma, American Journal of Clinical Pathology, Volume 132, Issue 5, November 2009, Pages 728–732,.