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PD-1 and PD-L1 expression on PBMC subsets in normal individuals and cancer patients

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Purpose

Immunotherapies aiming to interfere with the immune checkpoint molecule PD-1 (programmed death-1) and its ligand PD-L1 are currently being investigated in several clinical trials to treat cancer patients. The PD-1 pathway is one of the ways cancer cells evade immune-mediated killing. As little is known about the expression of PD-1 and PD-L1 in cancer patients compared to normal individuals, the aim of this study was to assess PBMC subsets for expression of these markers.

Methods

Twelve immune cell subsets were analyzed by flow-cytometry in 22 cancer patients and 16 normal individuals. The cancer patients consisted of 1 anal, 2 breast, 4 colon, 1 esophageal, 2 mesothelioma, 1 neuroendocrine, 1 non-small cell lung, 1 ovarian, 5 pancreatic, 3 renal cell and 1 squamous cell tracheal cancer patients. The subsets analyzed were CD4 and CD8 T cells, B cells, conventional dendritic cells (cDC), plasmacytoid DC (pDC), natural killer cells (NK), natural killer T cells (NKT), myeloid derived suppressor cell (MDSC), mono-

	CD4	CD8	B cell	Treg	cDC	pDC	NK	NKT	MDSC	mMDSC	gMDSC	Lin- MDSC
Subset (% PBMC)	=	=	↓	=	=	=	=	=	=	↓	↑	↑
PD-1+ (% parent)	↑	=	=	↑	↓	↑	=	=	↑	=	=	=
PD-L1+ (% parent)	=	=	=	↑	=	↑	↑	=	↑	=	=	↑

↑, increase frequency in cancer patients compared to normal individuals; ↓, decrease; =, no change
PBMC, peripheral blood mononuclear cell; B cells (CD19+); Treg (CD4+CD25+FoxP3+CD127-); cDC (CD3-CD56-CD1c+CD303-); pDC (CD3-CD56-CD1c-CD303+); NK (CD3-CD56+); NKT (CD3+CD56+); MDSC (CD11b+HLA DR-CD33+); mMDSC (CD14+CD15+MDSC); gMDSC (CD14-CD15+MDSC); Lin-MDSC (CD14-CD15+MDSC)

Figure 1 Differences in PBMC subsets and PD-1 and PD-L1 expression in cancer patients at baseline and normal individuals.

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cytic MDSC (mMDSC), granulocytic MDSC (gMDSC), and lineage-negative MDSC (Lin-MDSC). We also analyzed surface expression of PD-1 (clone MIH4) and PDL-1 (clone MIH1). See Figure 1.

Results

Compared to normal subjects, cancer patients had some PBMC subsets with changes in frequency but no differences in PD-1 and PD-L1 expression (i.e., B cells, mMDSCs, and gMDSCs). Other subsets showed changes in PD-1 and PD-L1 expression without differences in the frequency of the subset (i.e., CD4, Tregs, cDCs, pDCs, NK, and MDSCs). Lin-MDSCs presented at a higher frequency and greater PD-L1 positivity.

Conclusions

Understanding the differences of PBMC immune subsets between normal subjects and cancer patients, and the surface expression of PD-1 and PD-L1, can provide insights as to which immune subsets can be targeted by therapies aimed at interfering with the PD-1 pathway in cancer patients.

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