229 CX3CR1 IN EXHAUSTED CD8 T CELL STATES

[1]Apoorvi Chaudhri*, [2]Yunfei Wang, [3]Shao-Hsi Hung, [3]Gregory Lizee, [4]Ulrich Von Andrian, [2]Patrick Hwu, [5]Gordon Freeman. *[1]Dana-Farber Cancer Institute, Boston, MA, USA; MD Anderson Cancer Center, Houston, TX, USA; [2]Moffitt Cancer Center, Tampa, FL, USA; [3]MD Anderson Cancer Center, Houston, TX, USA; [4]Harvard Medical School, Boston, MA, USA; [5]Dana-Farber Cancer Institute, Boston, MA, USA*

Background Cancer has chronic antigen exposure that results in a suppressed CD8 T cell state termed exhaustion. An outcome of anti PD-1 blockade therapy is the expansion of early exhausted CD8+ T cells into a terminally differentiated exhausted state. The reversal of this transcriptionally plastic yet epigenetically fixed state of CD8 T cell exhaustion has the potential to increase responses to anti PD-1 therapy.

Methods CX3CR1 is a marker of CD8 T cell activation, effector function however less is known about the contribution of CX3CR1 in CD8 T cell exhaustion. We identified three distinct subsets of CD8+ tumor infiltrating lymphocytes (TILs) based on high, mid, and negative CX3CR1 expression in a mouse model of colon carcinoma.

Results The CX3CR1 high CD8+ T cells are more exhausted with higher PD1+TIM3+ expression compared to CX3CR1 mid and CX3CR1 negative cells thereby representing the terminal state of CD8 T cell exhaustion. Moreover, CX3CR1 high CD8 T cells increase following anti PD-1 blockade, and their abundance is associated with a positive response to anti PD-1.

Conclusions We identify a consequence of CX3CR1 in terminal T cell exhaustion, and our work can offer strategies to increase responses to anti PD-1.

Ethics Approval Animal experiments were performed as per the IACUC regulations at the Dana Farber cancer Institute, and the MD Anderson Cancer Center

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