CD160 in Cytotoxic T Cell Exhaustion and Its Effect on PD-1 Blockade Cancer Immunotherapy

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Cytotoxic T cells (CTLs) are lymphocytes capable of recognizing and attacking cancer cells. During continuous attacks, CTLs undergo an exhaustion process, gradually losing their abilities until they become dysfunctional. Cancer cells encourage CTL exhaustion by using inhibitory receptors, which suppress CTL function. Immunotherapy treatments that block the bonds between inhibitory receptors and their ligands have been developed in order to prevent CTL exhaustion, some of which have already been approved for clinical use; one example being PD-1 blockade, which blocks the bond between inhibitory receptor PD-1 and its ligand, PD-L1. Recent studies have suggested that other inhibitory receptors are involved in CTL exhaustion and impair the effectiveness of PD-1 blockade and similar treatments. The protein CD160 has been suggested as an inhibitory receptor potentially involved in the process. In this study, the role of CD160 has been examined in the exhaustion of melanoma-specific CTLs, as well as its effect on PD-1 blockade treatment. The results support the hypothesis that CD160 plays a role in CTL exhaustion, showing that CD160 knockout CTLs were less exhausted and more functional, both when treated with PD-1 blockade and without treatment. In addition, CD160 knockout CTLs had the potential to better communicate with dendritic cells. These results can lead to future studies, in which the possibility of CD160 blockade could be explored as an effective way to prevent CTL exhaustion during cancer, either by itself or in combination with existing immunotherapies, such as PD-1 blockade.

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