PD-1 Blockade Expands Intratumoral Memory T Cells - DTU Orbit (08/11/2017)

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Tumor responses to programmed cell death protein 1 (PD-1) blockade therapy are mediated by T cells, which we characterized in 102 tumor biopsies obtained from 53 patients treated with pembrolizumab, an antibody to PD-1. Biopsies were dissociated, and single-cell infiltrates were analyzed by multicolor flow cytometry using two computational approaches to resolve the leukocyte phenotypes at the single-cell level. There was a statistically significant increase in the frequency of T cells in patients who responded to therapy. The frequency of intratumoral B cells and monocytic myeloid-derived suppressor cells significantly increased in patients' biopsies taken on treatment. The percentage of cells with a regulatory T-cell phenotype, monocytes, and natural killer cells did not change while on PD-1 blockade therapy. $CD8^+$ memory T cells were the most prominent phenotype that expanded intratumorally on therapy. However, the frequency of $CD4^+$ effector memory T cells significantly decreased on treatment, whereas $CD4^+$ effector T cells significantly increased in nonresponding tumors on therapy. In peripheral blood, an unusual population of blood cells expressing CD56 was detected in two patients with regressing melanoma. In conclusion, PD-1 blockade increases the frequency of T cells, B cells, and myeloid-derived suppressor cells in tumors, with the $CD8^+$ effector memory T-cell subset being the major T-cell phenotype expanded in patients with a response to therapy.

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