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Sommario	Abstract The immune system plays a major role in the surveillance against tumors. Tumor cells develop different strategies to escape immune surveillance, while immune therapies are designed to overcome mechanisms that mediate tolerance to tumor cells.The cell-cycle inhibitor p21 regulates immune tolerance, as revealed by the susceptibility of p21-deficient (p21-/-) mice to develop mild autoimmune diseases. My host-lab has reported that p21-/- myeloid leukemias are unable to transplant into syngeneic mice. I demonstrated that the same phenotype applies to p21-/- breast cancers, and that p21-/- tumors reacquire transplantability when injected into immunodeficient mice. Thus, I investigated cellular and molecular mechanisms underlying the effect of p21 in evading the immune surveillance against breast cancer. I showed that depletion of p21 selectively in CD11b+c+ antigen presenting cells (APCs) induces a robust MHCII-dependent and antigen-independent proliferation of CD4+ lymphocytes endowed with effector/memory phenotype and potent anti-tumor activities, mimicking homeostatic proliferation of T cells. Single-cell RNA sequencing of WT and p21-/- CD11b+c+ APCs showed differential expression of genes encoding antigen-processing and -presentation membrane proteins. Notably, I showed that p21-/- CD11b+ APC cells (comprising ~50% of the

	CD11b+c+ subpopulation) can be used in vitro to generate T cells with potent anti-cancer effect in vivo, thus paving the way to novel anti-cancer immunotherapeutic approaches in humans.
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