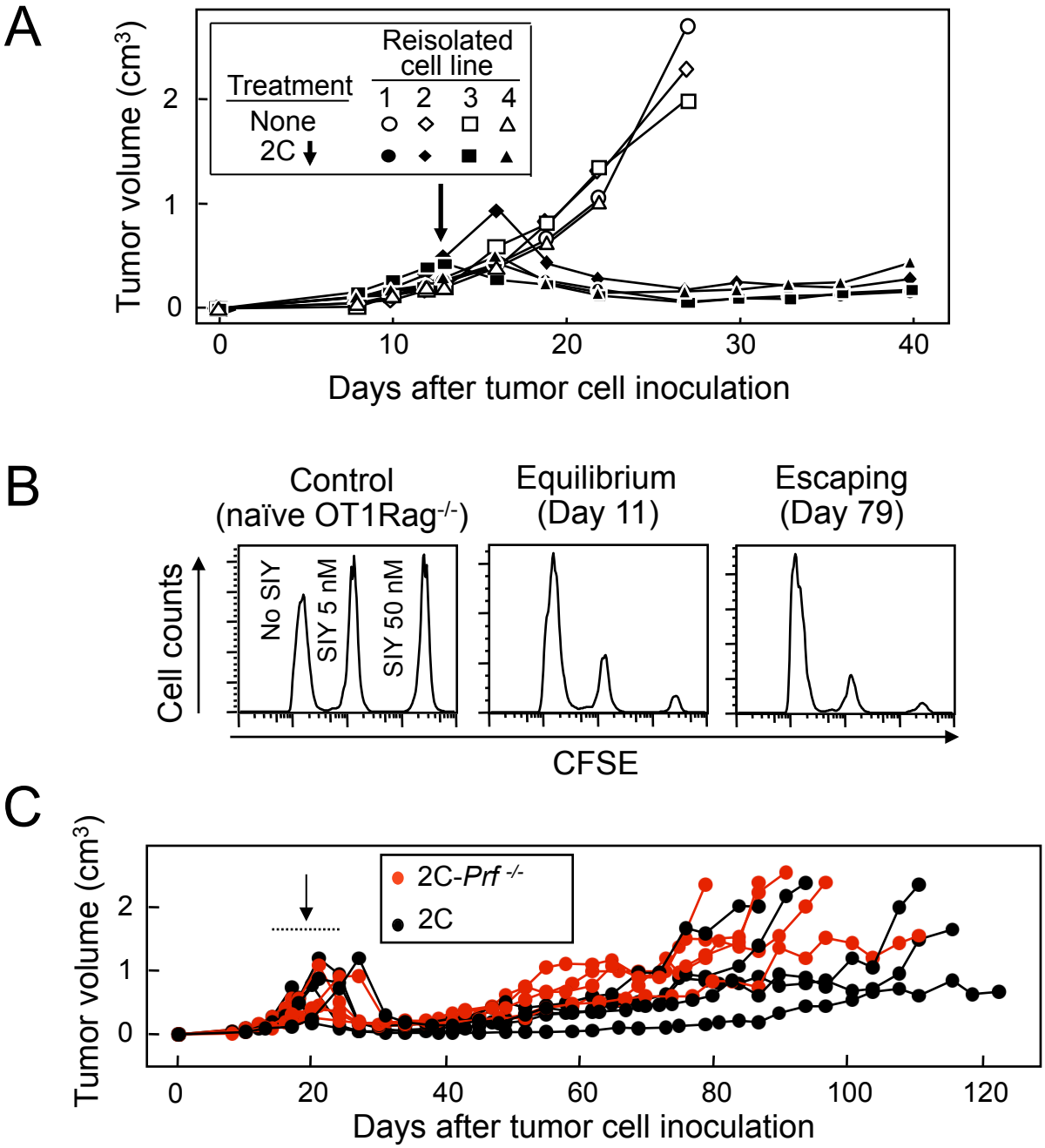
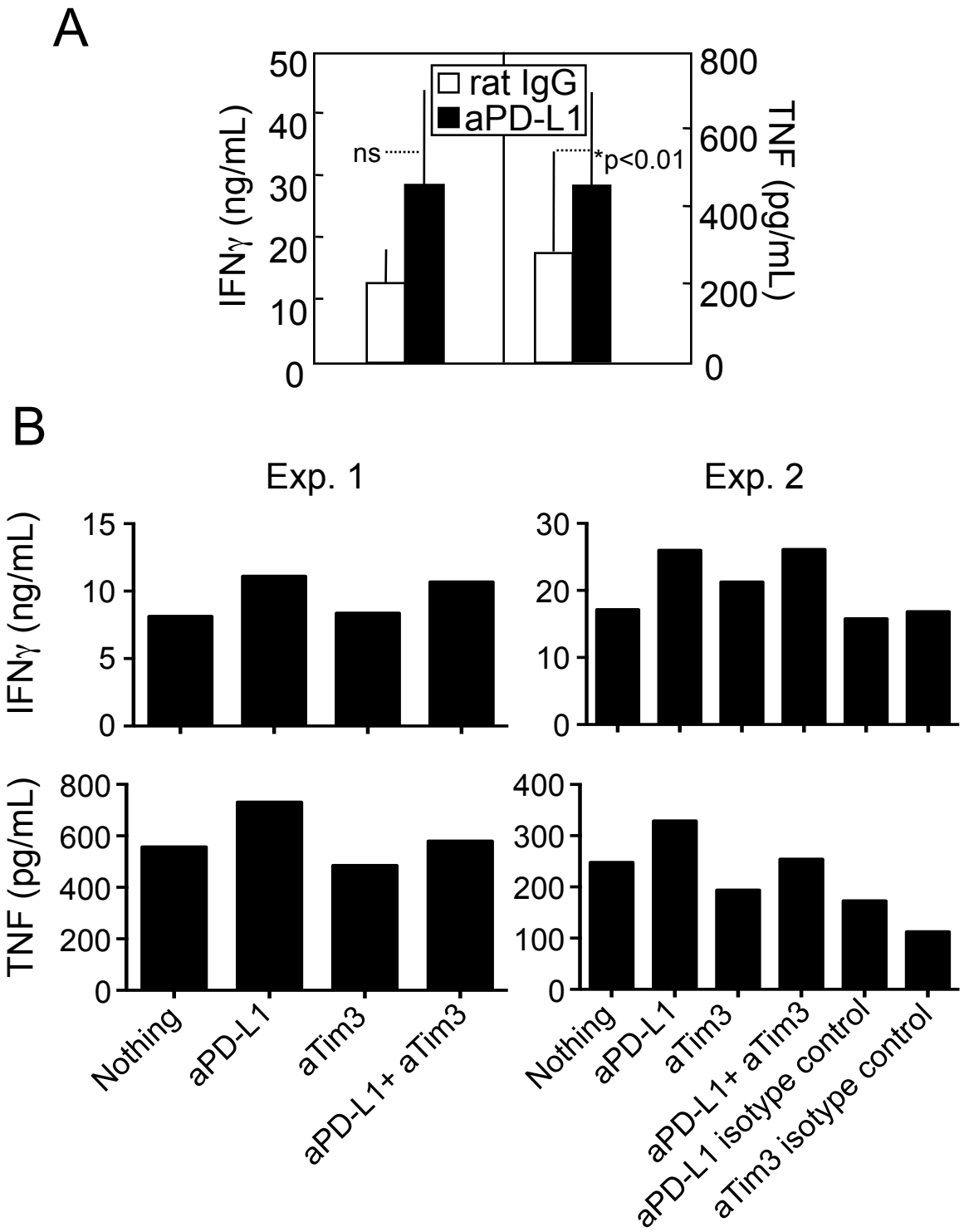
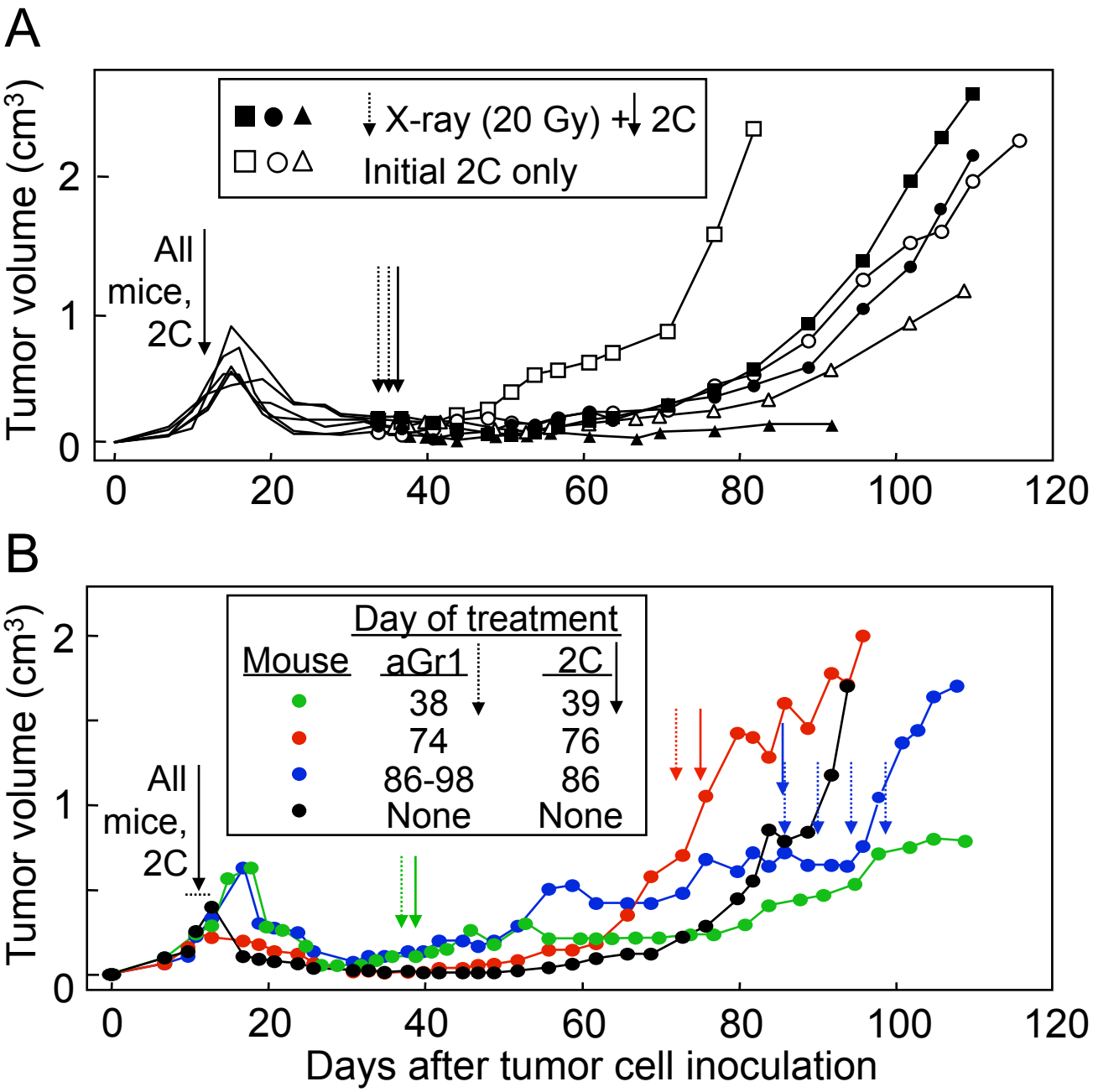


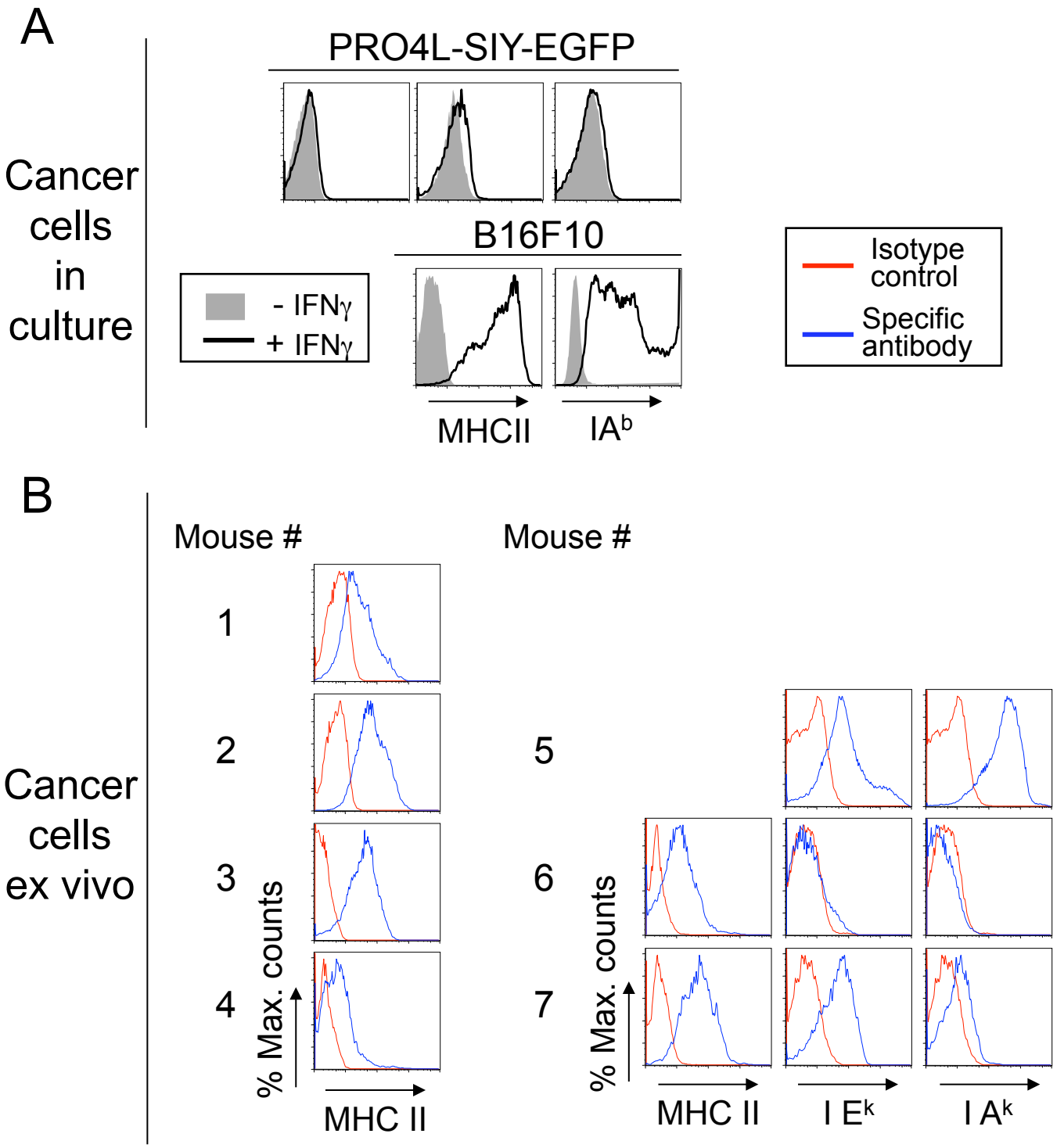
Suppl. Figure 1. A. Tumors that escape an equilibrium caused by CD8 T cells targeting tumor stroma are not Ag-loss variants. Four PRO4L-SIY-EGFP tumors that escaped therapy with 2C T cells were reisolated and adapted into culture. Each reisolated cell line was injected into two OT1Rag$^{-/-}$ mice. Out of these two recipients, one was treated with 2C cells, and one was left untreated as indicated. **B. The Ag-specific lytic function of 2C cells in vivo has not declined in mice bearing escaping tumors.** A 5 h in vivo killing assay was performed in a mouse bearing a PRO4L-SIY-EGFP tumor kept in stable size by 2C cells (day 11 since treatment) and a mouse with an escaping tumor (day 79). Representative examples are shown from 2 experiments with a total of 7 animals (2 controls, 2 mice in equilibrium, 3 mice escaping equilibrium). **C. Equilibrium can be achieved in mice lacking perforin.** PRO4L-SIY-EGFP tumor-bearing mice were treated between day 14-24 (dotted line) with perforin-deficient 2C cells (2C- *prf*$^{-/-}$) or normal 2C cells (2 pooled independent experiments and 5 total animals per group). In all ten animals, tumor equilibrium as defined in Fig. 3 legend was established.



Suppl. Figure 2. PD-L1 but not Tim3 blocking in vitro partially reverses the ability of tumor-infiltrating CD8$^+$ T cells to produce cytokines. 2C cells from tumors escaping equilibrium were re-stimulated in vitro with SIY peptide for 3 days in the presence of anti-PD-L1, anti-Tim3 or isotype control immunoglobulin. TNF and IFNγ in the supernatants were measured by ELISA. A. Summary data are pooled from 3 independent experiments testing anti-PD-L1 blocking. IFNγ production shows a trend to increase by blocking PD-1/PD-L1 interaction although it is not statistically significant. B. Two individual experiments are shown where either anti-PD-L1 (aPD-L1), anti-Tim3 (aTim3) or both antibodies were added to the in vitro culture. Tim3 blocking did not further improve the effect of PD-L1 blocking.



Suppl. Figure 3. A second transfer of CD8⁺ T cells following tumor irradiation or anti-Gr1 antibody therapy cannot prevent tumor escape. A. Mice with tumors in equilibrium induced by a first dose of 2C cells were treated with 2 doses (20 Gy each, 24 h apart) of local radiotherapy followed by a second dose of 2C cells one day later. Data are from 3 independent experiments and 6 total mice**. B.** Mice with tumors in equilibrium or escaping equilibrium were treated with one or more doses of anti-Gr1 (aGr1) depleting antibody, followed by a second dose of 2C cells, as indicated in the insert. Results pooled from 2 independent experiments and 4 total mice are shown.



Suppl. Figure 4. Cancer cells are negative for MHC-II in vitro but can up-regulate MHC-II in tumors in vivo. A. PRO4L-SIY-EGFP cells are negative for MHC-II in vitro, even after incubation with IFNγ for 72 h. As a control, B16F10 cell line was used in parallel and found to up-regulate MHC-II expression as expected. **B.** The same cancer cells were analyzed ex vivo, from mice bearing tumors escaping control by 2C cells. Each plot represents an individual mouse from a total of 6 experiments. The anti-MHC II antibody used recognizes a polymorphic determinant shared by several MHC II molecules including I-A^b and I-E^k. Antibodies recognizing only the specific MHC II molecules were used in parallel in some experiments.