**Supplemental data**

**Supplemental figure 1: effect of Aldara on immune cell activation and in other tumor models**

A) Tumor bearing mice were treated with IL-2 alone, Aldara alone or the combination. Tumor outgrowth was followed. Data from one experiment with four mice per group. Arrow indicates time of treatment. B) CD69 expression was measured on NK cells in blood of mice in different treatment groups. Data is shown from one experiment as mean and SEM with 3 mice per group. Arrows indicate time of treatment. C) Frequencies of myeloid cells was measured in blood of mice with only tumor, treatment only or tumor-treated mice. Data is shown as mean and SEM from one experiment with 2-3 mice per group. Arrows indicate time of treatment. D) Seven days after tumor challenge, tumors of mice were harvested and an ICS was performed. Shown are pooled data from two independent experiments with 3-4 mice per group. (Student t test, n.s.= non-significant). E and F) Mice were inoculated with B16 (D) or B78H1 tumors (E) and treated with Aldara on the opposite flank. Data shown from two independent experiments with 4 mice per group. Log-rank (Mantel Cox) analysis, \*\* P<0.01.

**Supplemental figure 2: Class I and II upregulation, effect type I IFN signalling and late depletions**

A) NK cell depletion was inefficient immediately after Aldara treatment. NK cell frequency was followed in blood upon depletion. Data is representative for at least three independent experiments. B and C) RMA-S cells and B16 cells were stimulated *in vitro* with IFNγ or type I IFN and expression levels of MHC-I and MHC-II was determined by flow cytometry. Data representative of two independent experiments. D) IFNAR signalling was blocked around the time of Aldara treatment, tumor size was followed. Shown is data from two independent experiment with 4-6 mice per group, mean + SEM. Two-way ANOVA, \*P<0.05, n.s.= non-significant. E) Depletion of CD4+, CD8+ T or NK cells was started at day 6 after the last treatment time point, when tumors underwent successful regressions.

**Supplemental figure 3: immune cell composition after Aldara treatment**

Tumor-bearing mice were treated with Aldara and early (day 14) or late (day 18) after tumor inoculation, tumor and lymphoid organs were analyzed. As a control, untreated mice were used, bearing comparable sizes of tumors. Shown are the frequency of eosinophils, macrophages or neutrophils within CD45+ population, in tumor or spleen. Data is shown as mean with SEM and is pooled from two or three experiments with 3 mice per group. B) Frequency of CD4+ T cells, CD8+ T cells, NK cells or CD11b+ cells within CD45+ cells in dLN of mice. C) Phenotype of intratumoral CD4+ T cells at day 18 after tumor inoculation, determined by flow cytometry. Data from two independent experiments with 3 mice per group, shown as mean and SEM. Student t-test, \*\*\*P< 0.001.

**Supplemental figure 4: T cell phenotype after treatment**

A) Over time, blood was taken from mice and incubated overnight in the presence of a control helper peptide. Cytokine production by CD4+T cells was analyzed by ICS the following day. Data from one experiment with four mice per group, shown as mean and SEM. B) Splenocytes from treated mice were cultured overnight on unloaded or EnvH loaded D1 cells and cytokines were measured by a 23-plex luminex assay. Data is pooled from two independent experiments with three mice per group. C and D) Cytokine expression of CD8+ T cells in spleen or tumor of untreated and treated mice. Data is pooled from two or three independent experiments with 3 mice per group. (Two way ANOVA, n.s.= non-significant, \*P<0.05). E) Activation status of CD4+ or CD8+ T cells was followed in blood after Aldara treatment (arrows indicate time of treatment). Shown are results from one experiment with three mice per group. F) Naive, wildtype CD4+ T cells were stimulated with CD3 and CD28 antibodies or type I IFN and CXCL10 levels were determined by qPCR. Data is shown from one of two independent experiments with comparable results, as mean and SD. Expression relative to the household genes GAPDH and YWHAZ.