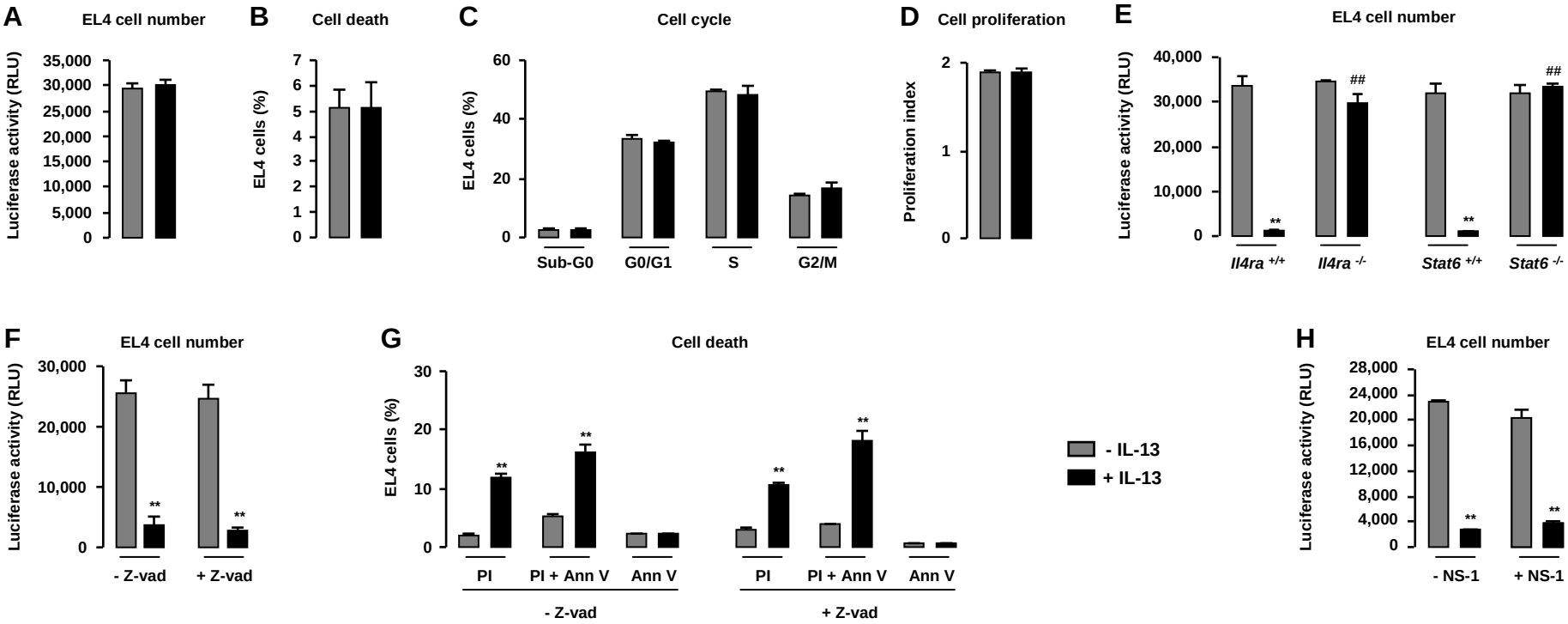
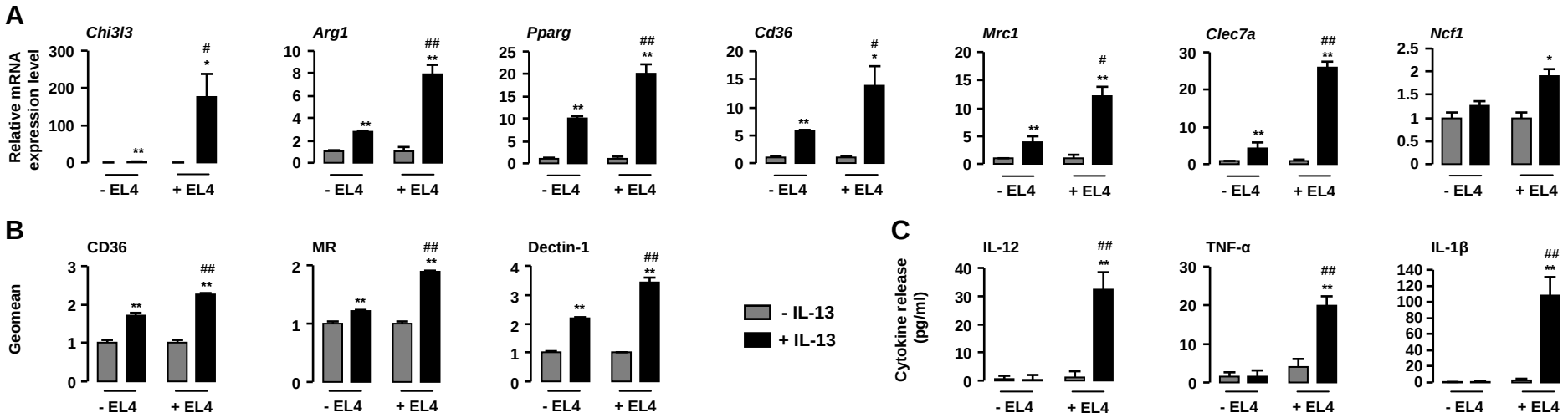
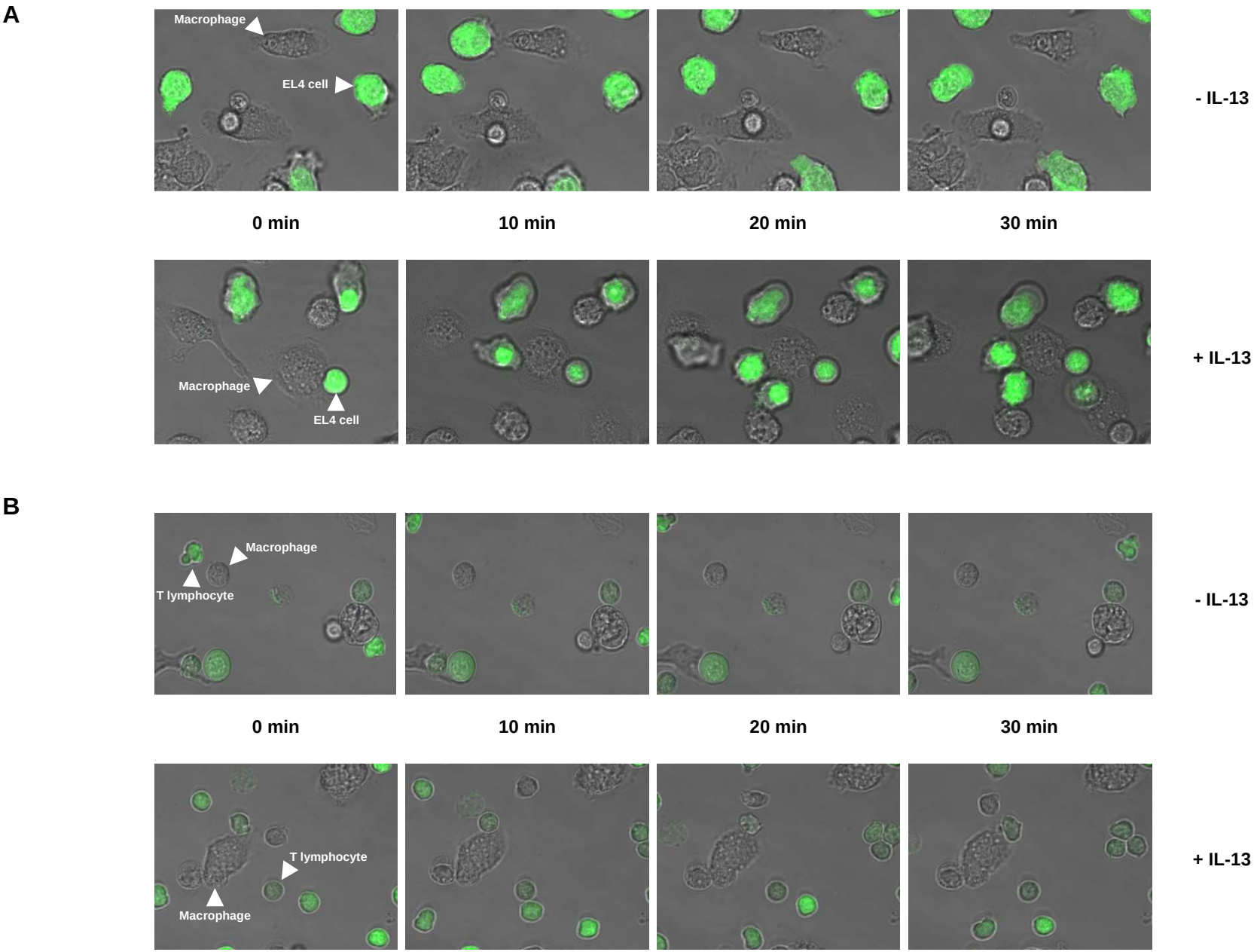


Supplementary Figure 1. IL-13 induces caspase independent necrosis of EL4 tumor cells through IL-13 receptor-coupled STAT-6 signaling in macrophages. A-**D**, number (**A**), cell death (**B**), cell cycle (**C**) and cell proliferation (**D**) of EL4-luc2 cultured in presence or not of IL-13 were respectively determined by the quantification of bioluminescence intensity and by flow cytometry using annexin-V/PI staining, PI DNA staining and fluorescent dye CFSE. **E**, number of EL4-luc2 cells cultured in presence of untreated or IL-13-treated peritoneal macrophages from *Il4ra-/-* or *Stat6-/-* mice and their corresponding WT counterpart (*Il4r+/+* or *Stat6+/+*). **F** and **G**, number (**F**) and cell death (**G**) of EL4-luc2 in presence of macrophages treated or not with IL-13 in presence or not of Z-vad. (**H**) number of EL4-luc2 in presence of macrophages treated or not with IL-13 in presence or not of Necrostatin-1. Results correspond to mean ± SEM of triplicates and are representative of at least three independent experiments. **p < 0.01 compared to respective untreated macrophages and ##p < 0.01 compared to IL-13-treated WT littermate. P values were determined using Bonferroni-Dunnett method.



Supplementary Figure 2. The physical contact with EL4 tumor cells switches IL-13-activated macrophages toward cytotoxic phenotype characterized by a pro-inflammatory signature. A, gene expression analysis of polarization markers in untreated or IL-13-treated macrophages in presence or not of EL4-luc2 cells, determined using RT-PCR. **B**, cell-surface protein levels for the indicated receptors in untreated or IL-13-treated macrophages in presence or not of EL4-luc2 cells were quantified by flow cytometry. **C**, cytokine production of untreated or IL-13-treated macrophages in presence or not of EL4-luc2 cells was quantified by ELISA. For geomean fluorescence and mRNA expression, data are expressed as fold induction relative to the corresponding untreated macrophages. Results correspond to mean ± SEM of triplicates and are representative of at least three independent experiments. *p < 0.05, **p < 0.01 compared to the respective untreated macrophages, #p < 0.05, ##p < 0.01 compared to IL-13-treated macrophages without EL4. P values were determined using Bonferroni-Dunnett method.

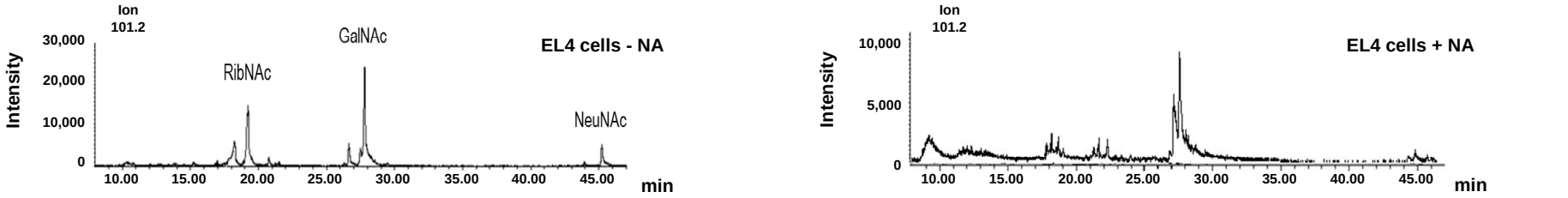


Supplementary Figure 3. IL-13-activated macrophages strongly bind EL4 tumor cells and not normal T lymphocytes. A and **B**, EL4 tumor cells (**A**) and mouse normal T cells (**B**) were labeled with CFSE, co-cultured with untreated or IL-13-treated macrophages and observed by confocal microscopy. The images (40X) were assessed after 0, 10, 20 and 30 min of co-culture. Results are representative of at least three independent experiments.

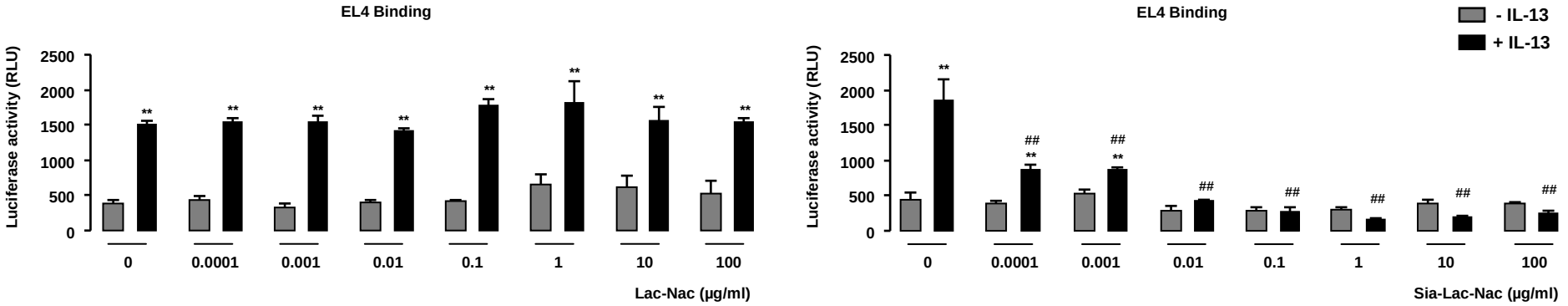
A

	Fucosamine	Quinovosamine	Glucosamine	Galactosamine	Mannosamine	N-Acetyl-Galactosamine (GalNAc)	N-Acetyl-Neuraminic acid (NeuNAC)
LT	14	8	31	37	30	4	6
EL4 cells	16	4	32	32	28	38	40

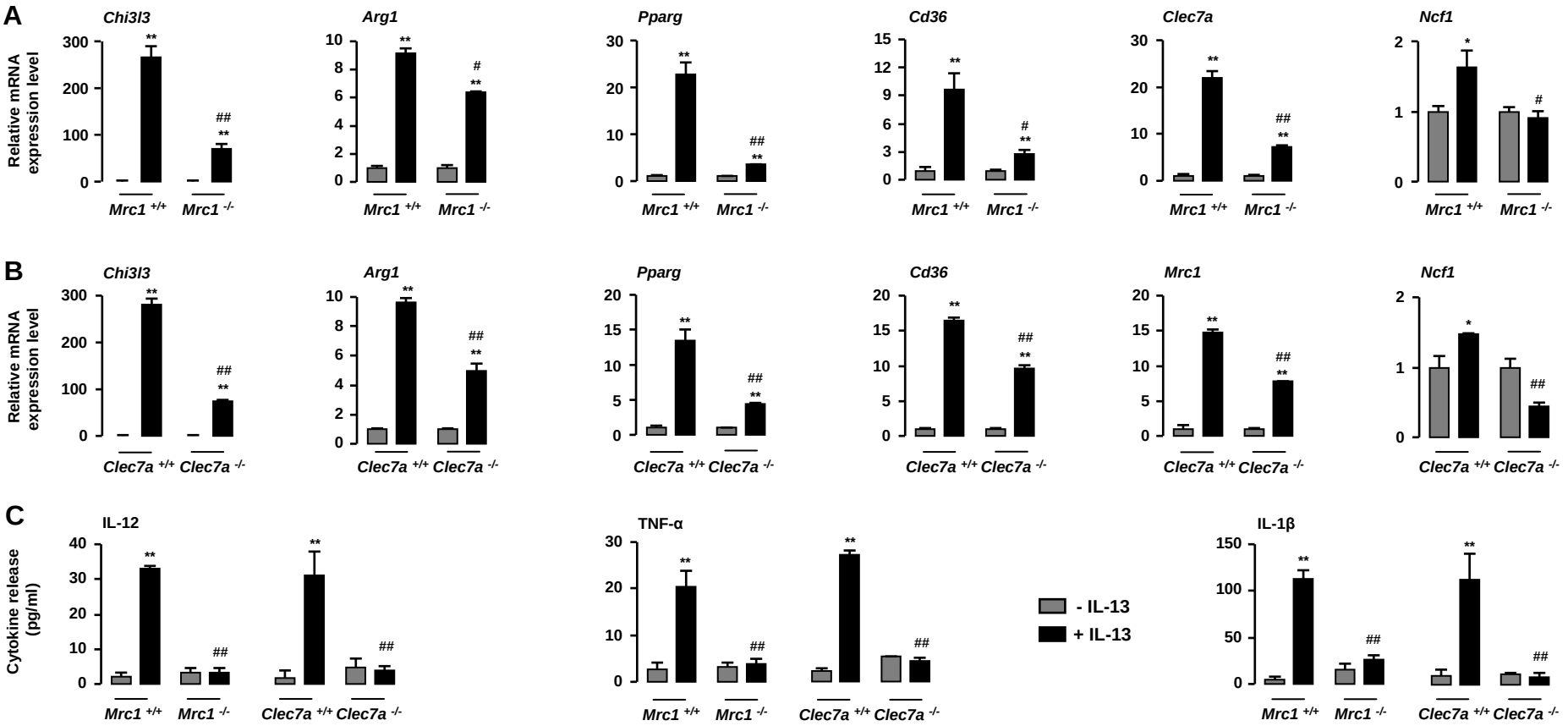
B



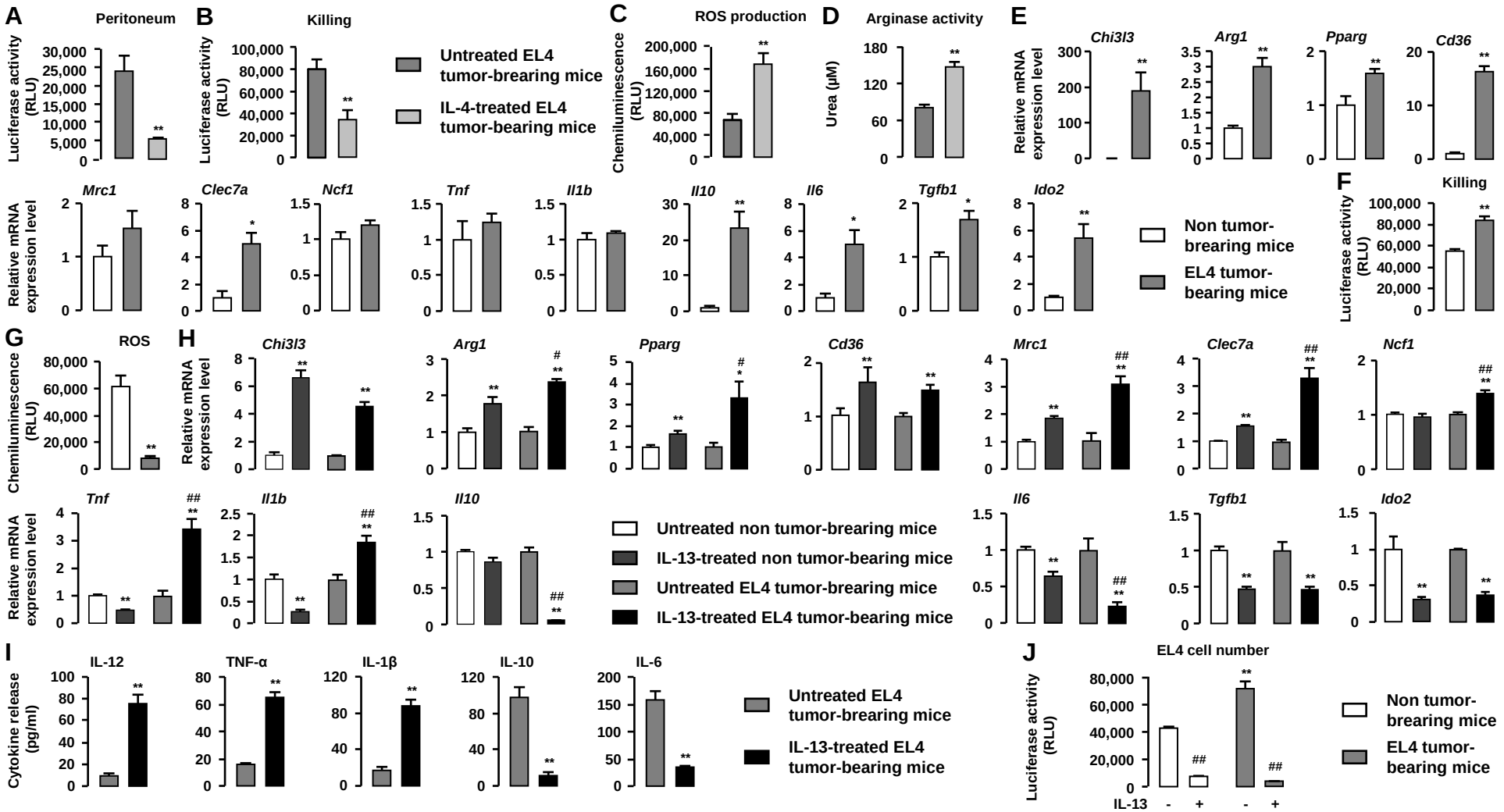
C



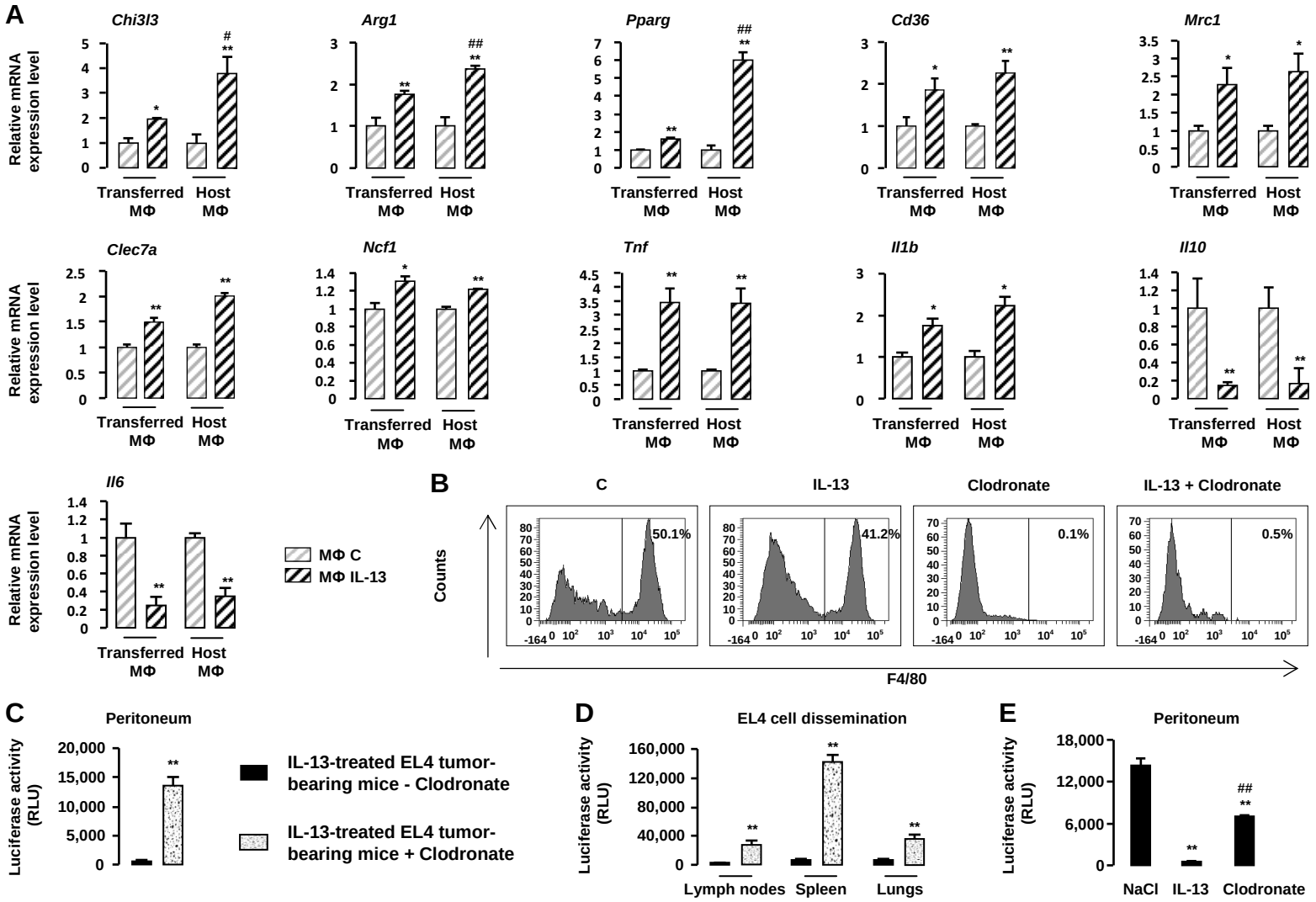
Supplementary Figure 4. Sialic acid is the critical epitope at the surface of EL4 cells responsible of their interaction with IL-13-activated macrophages. **A**, carbohydrate relative amounts at the surface of T lymphocytes and EL4 cells, obtained by EI+ GC-MS measurements. Numbers are intensities x104. Deviations over 3 essays were +/- 5 104. **B**, chromatogram of ion m/z 101 specific of acetylated and methylated amino-sugars at the surface of EL4 cells pretreated or not with NA. Numbers are intensities x104. **C**, binding of EL4-luc2 cells on IL-13-stimulated macrophages pre-treated or not with Lac-Nac (N-acetyllactosamine) and Sia-Lac-Nac (Sialyl-N-acetyllactosamine) using luminescence assay. Results correspond to mean ± SEM of triplicates and are representative of at least three independent experiments. *p < 0.05, **p < 0.01 compared to respective untreated macrophages and #p < 0.05, ##p < 0.01 compared to IL-13-treated macrophages without Lac-Nac and Sia-Lac-Nac. P values were determined using Bonferroni-Dunnett method.



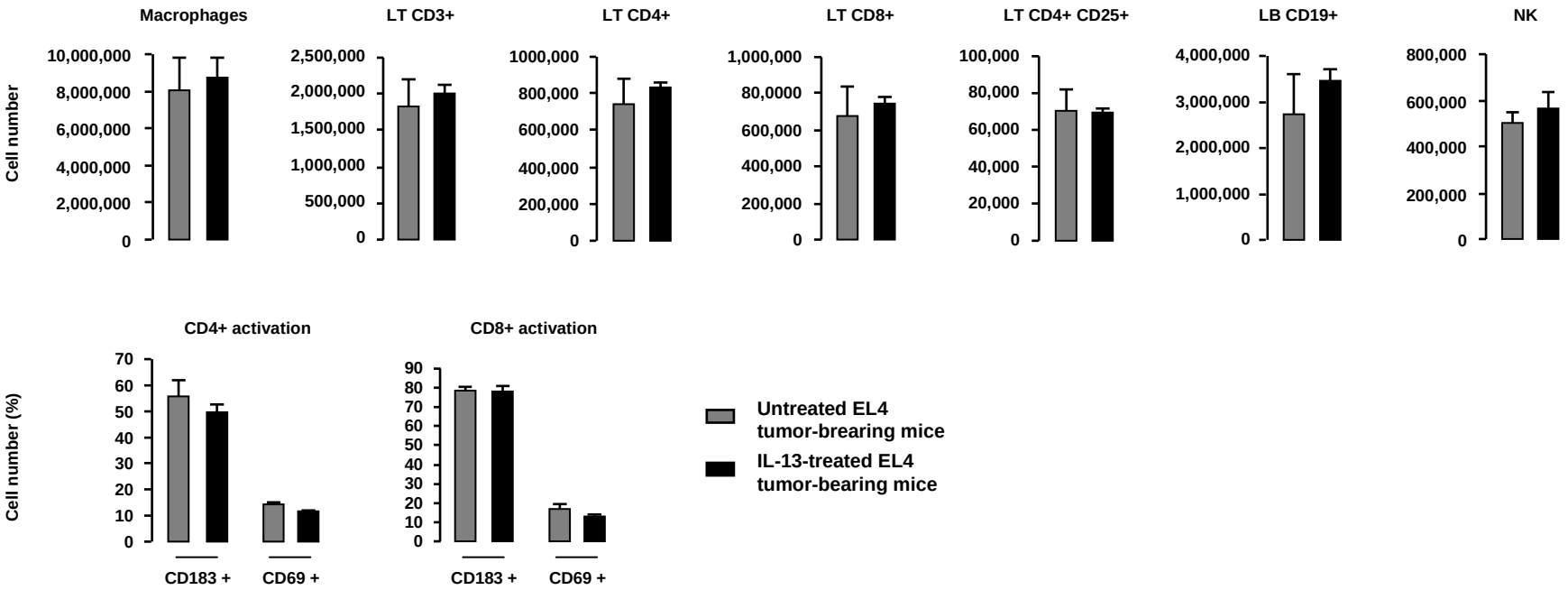
Supplementary Figure 5. The switch of IL-13-activated macrophages toward cytotoxic phenotype requires both MR and Dectin-1. A and **B**, gene expression analysis of polarization markers in untreated or IL-13-treated macrophages from *Mrc1-/-* (**A**) or *Clec7a-/-* (**B**) mice and their corresponding WT counterpart (*Mrc1*+/+ or *Clec7a*+/+) in response to EL4-luc2 cells, determined using RT-PCR. Data are expressed as fold induction relative to the corresponding untreated macrophages. **C**, cytokine production of untreated or IL-13-treated macrophages from *Mrc1-/-* or *Clec7a-/-* mice and their corresponding WT counterpart (*Mrc1*+/+ or *Clec7a*+/+) in response to EL4-luc2 cells were quantified by ELISA. Results correspond to mean ± SEM of triplicates and are representative of at least three independent experiments. *p < 0.05, **p < 0.01 compared to respective untreated macrophages and #p < 0.05, ##p < 0.01 compared to IL-13-treated WT littermate. P values were determined using Bonferroni-Dunnett method.



Supplementary Figure 6. IL-4 treatment inhibits T-cell lymphoma progression and enhances macrophage antitumor properties. A-D, C57BL/6 mice were injected intraperitoneally with 1 × 106 EL4-luc2 tumor cells and the following day the mice were treated or not by i.p. with IL-4. **A,** Tumor burden in ascites of untreated and IL-4-treated EL4 tumor-bearing mice was determined by the quantification of bioluminescence intensity. **B-D**, killing activity (**B**), ROS production (**C**) and arginase activity (**D**) of peritoneal macrophages collected on day 12 from untreated and IL-4-treated EL4 tumor-bearing mice were determined respectively by the quantification of bioluminescence intensity, chemiluminescence intensity and urea generation. **Characterization of macrophages from ascites of EL4 tumor-bearing mice. E-G** and **J,** C57BL/6 mice were injected with 1 x 106 EL4-luc2 cells or NaCl and peritoneal macrophages were collected on day-12. **E**, gene expression analysis of polarization markers in peritoneal macrophages from non-tumor-bearing mice or EL4 tumor-bearing mice was determined using RT-PCR. mRNA expression are represented in fold induction relative to mRNA expression for the corresponding macrophages from non-tumor-bearing mice. **F**, killing activity against EL4 cells of peritoneal macrophages from non-tumor-bearing mice or EL4 tumor-bearing mice was determined by the quantification of bioluminescence intensity. **G**, ROS production of peritoneal macrophages from non-tumor-bearing mice or EL4 tumor-bearing mice was determined by the quantification of chemiluminescence intensity. **H** and **I**, C57BL/6 mice were injected intraperitoneally with 1 × 106 EL4-luc2 tumor cells and the following day the mice were treated or not by i.p. with IL-13. **H**, gene expression analysis of polarization markers of peritoneal macrophages collected on day 12 from non tumor or tumor-bearing mice treated or not with IL-13 was determined by RT-PCR. mRNA expression are represented in fold induction relative to the mRNA expression for the corresponding macrophages from untreated mice. **I**, cytokine production in ascites collected on day-12 from untreated and IL-13-treated EL4 tumor-bearing mice were quantified by ELISA. **J**, number of EL4-luc2 cells cultured in presence of peritoneal macrophages from non-tumor-bearing mice or EL4 tumor-bearing mice treated or not *ex vivo* with IL-13. Results correspond to mean ± SEM and are representative of at least three independent experiments. **p < 0.01 compared to respective untreated EL4 tumor-bearing mice or to respective macrophages from non-tumor-bearing mice and ##p < 0.01 compared to respective IL-13-treated non tumor-bearing mice or respective IL-13-untreated macrophages. P values were determined using Bonferroni-Dunnett method.



Supplementary Figure 7. IL-13-activated macrophages had a relevant functional consequence on T-cell lymphoma development. A, Gene expression analysis of polarization markers of transferred (F4/80+ MHC-2+ Cell trace+) and host (F4/80+ MHC-2+ Cell trace-) macrophages collected on day 12 from EL4 tumor-bearing mice injected with macrophages harvested from untreated C57BL/6 (MΦ C) or IL-13-treated mice (MΦ IL-13). (**B**-**D**), C57BL/6 mice were injected with 1 x 106 EL4-luc2 cells and treated *i.p.* by IL-13. Macrophage depletion was performed by clodronate *i.p.* administration. **B**, quantification of F4/80 positive cells in ascites from EL4 tumor-bearing mice and IL-13-treated EL4 tumor-bearing mice by flow cytometry. **C** and **D**, number of EL4-luc2 cells in peritoneum (**B**), in lymph nodes, spleen and lungs (**C**) of IL-13-treated EL4 tumor-bearing mice injected or not with clodronate were determined by the quantification of bioluminescence intensity. **E**, number of EL4-luc2 cells in peritoneum of EL4 tumor-bearing mice treated or not with IL-13 or clodronate from day 3 post-tumor injection. *p < 0.05 and **p < 0.01 compared to respective macrophages harvested from untreated mice, IL-13-treated EL4 tumor-bearing mice without clodronate or untreated mice (NaCl) and, $^{\#}$p < 0.05 and $^{\#\#}$p < 0.01 compared to respective transferred macrophages harvested from IL-13-treated mice or IL-13-treated EL4-tumor bearing mice. P values were determined using Bonferroni-Dunnett method.



Supplementary Figure 8. IL-13 administration to EL4 tumor bearing mice did not impact the tumor adaptive immunity. Number of immune cells infiltrated in peritoneal cavity of untreated and IL-13-treated EL4 tumor-bearing mice at day 12 post-injection by flow cytometry.