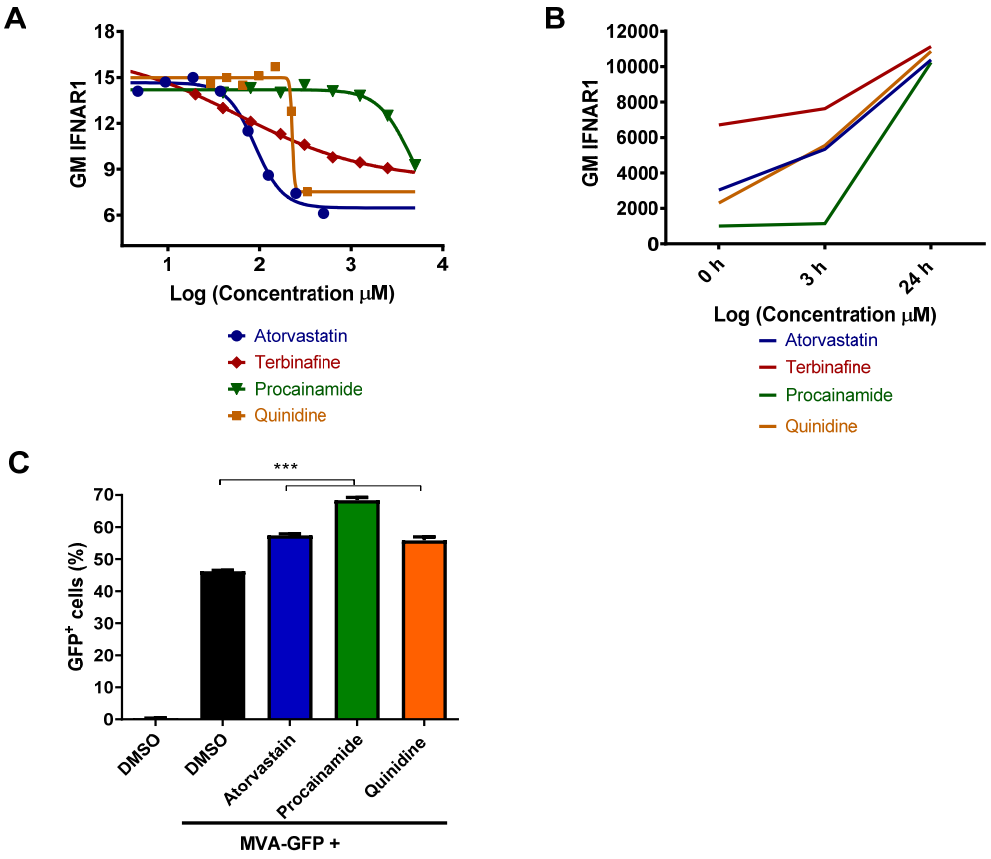
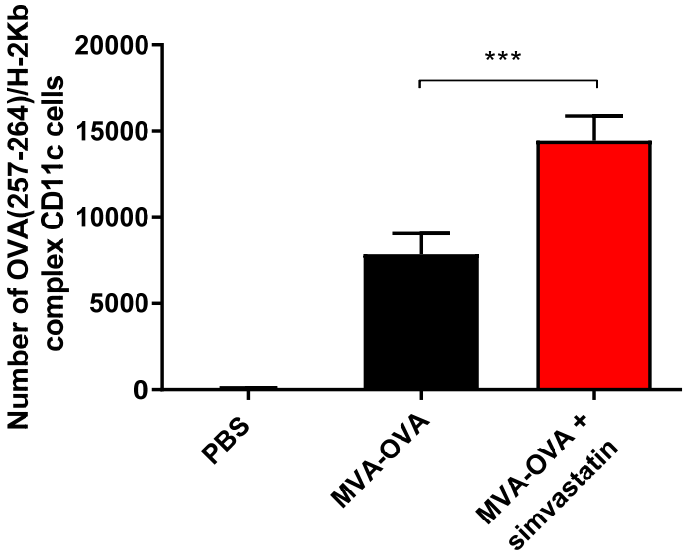
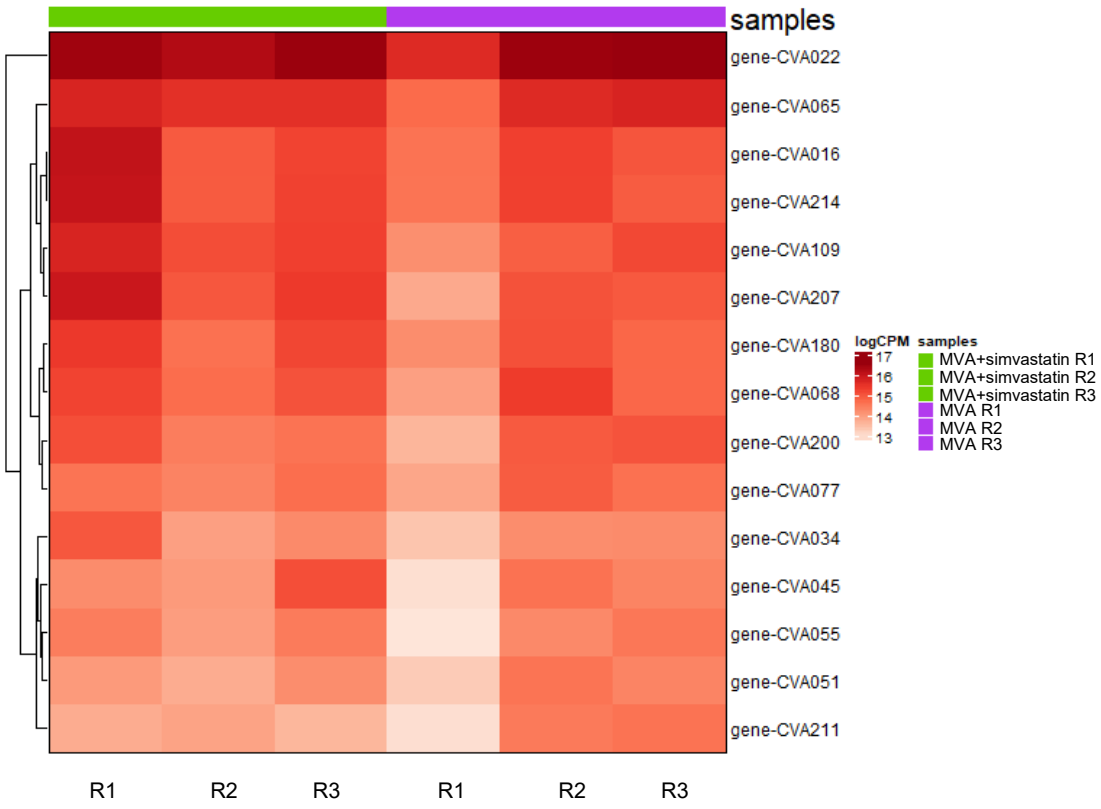


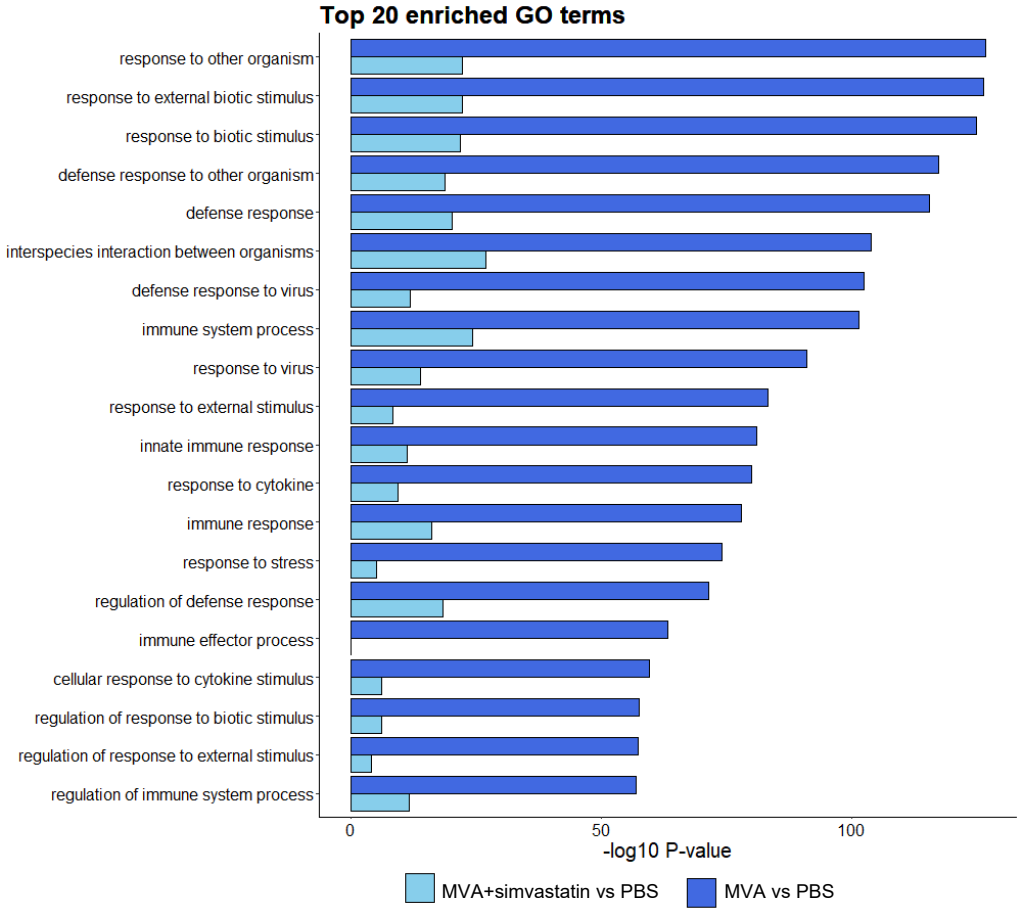
Supplementary Figure 1. Drugs that reduce surface expression of IFNR1 and protein endocytosis. L929 cells were incubated with different concentrations of atorvastatin, terbinafine, procainamide, and quinidine for 3 hours. Then, A) levels of IFNR1 on the cell membrane were quantified by flow cytometry. B) BSA-FITC internalization was quantified by flow cytometry. GM, geometric mean. C) Percentage of GFP positive cells 24 hours after infection with MVA-GFP at 10 MOI.



Supplementary Figure 2. Simvastatin enhances the number of dendritic cells with OVA-derived peptide bound to MHC class I upon MVA-OVA infection. Mouse dendritic cells were purified from spleen with CD11c magnetic microbeads. 100000 dendritic cells were infected with MVA-OVA at 1 MOI in the presence or not of simvastatin (1 μM). 24 hour later, the number of dendritic cells presenting an OVA-derived peptide in MHC class I was detected by flow cytometry staining with 25D1 antibody.



Supplementary Figure 3. Heatmap of highly expressed MVA genes. B16-OVA melanoma cells were injected subcutaneously. Seven days later, mice were treated intraperitoneally (i.p) with vehicle or simvastatin (20 µg/mice). After 2 hours, MVA-OVA ($5x10^7$ TCID50 per mouse) was administered peritumorally (p.t.). Four hours later, mice were sacrificed, and tumor mRNA was analyzed by RNAseq. The heatmap represents the cluster of highly expressed MVA genes in the group treated with MVA-OVA alone or in the group treated with the combination MVA-OVA+simvastatin.



Supplementary Figure 4. Top 20 enriched GO terms for MVA+simvastatin vs PBS and MVA versus PBS. B16-OVA melanoma cells were injected subcutaneously. Seven days later, mice were treated intraperitoneally (i.p) with vehicle or simvastatin (20 µg/mice). After 2 hours, MVA-OVA ($5x10^7$ TCID50 per mouse) was administered peritumorally (p.t.). Four hours later, mice were sacrificed, and tumor mRNA was analyzed by RNAseq. Bars represent the differential pathways based on the p-value.

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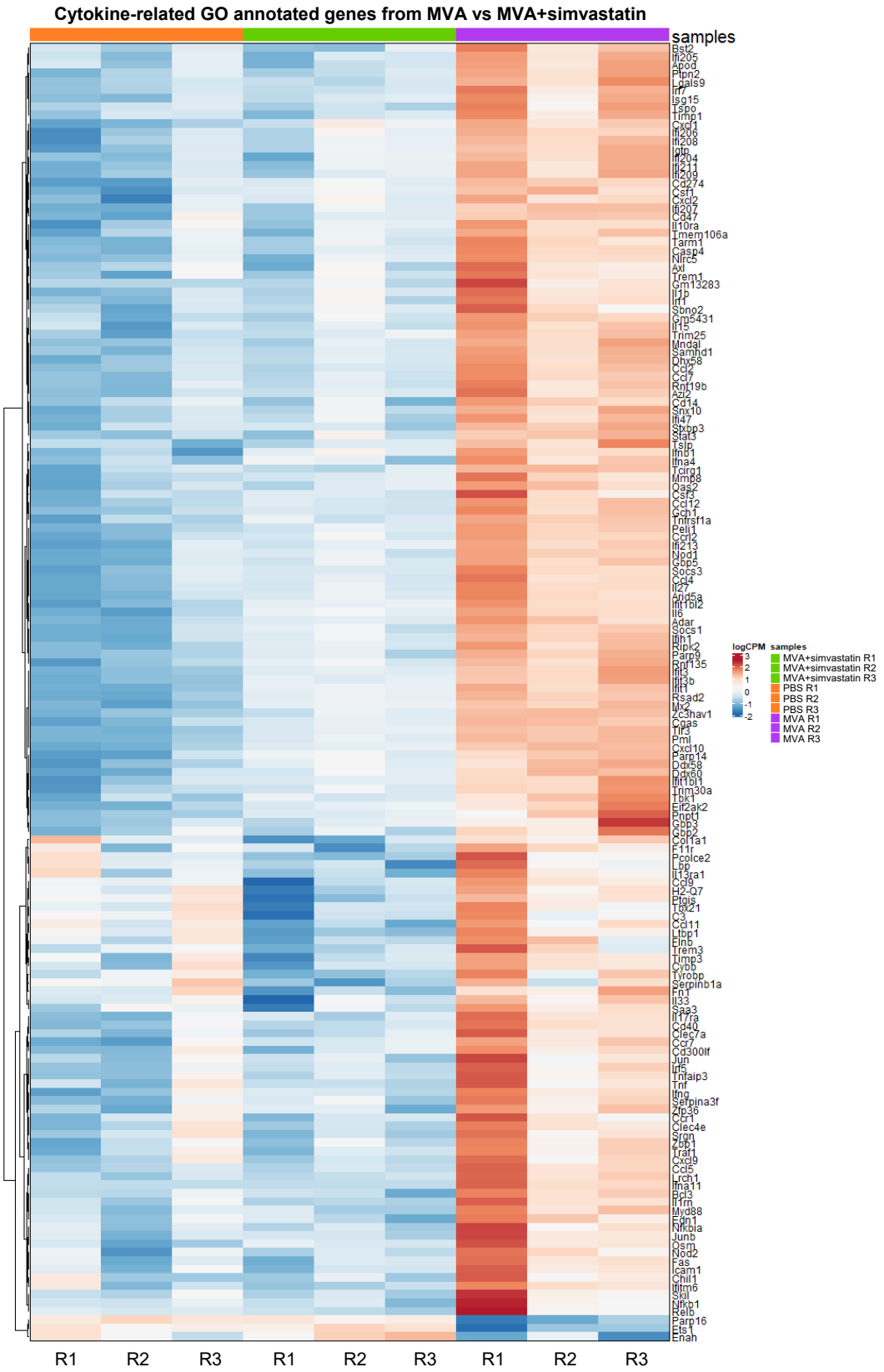
Cytokine-related GO annotated genes from MVA vs MVA+simvastatin
samples
logCPM
samples
MVA+simvastatin R1
MVA+simvastatin R2
MVA+simvastatin R3
PBS R1
PBS R2
PBS R3
MVA R1
MVA R2
MVA R3
R1
R2
R3
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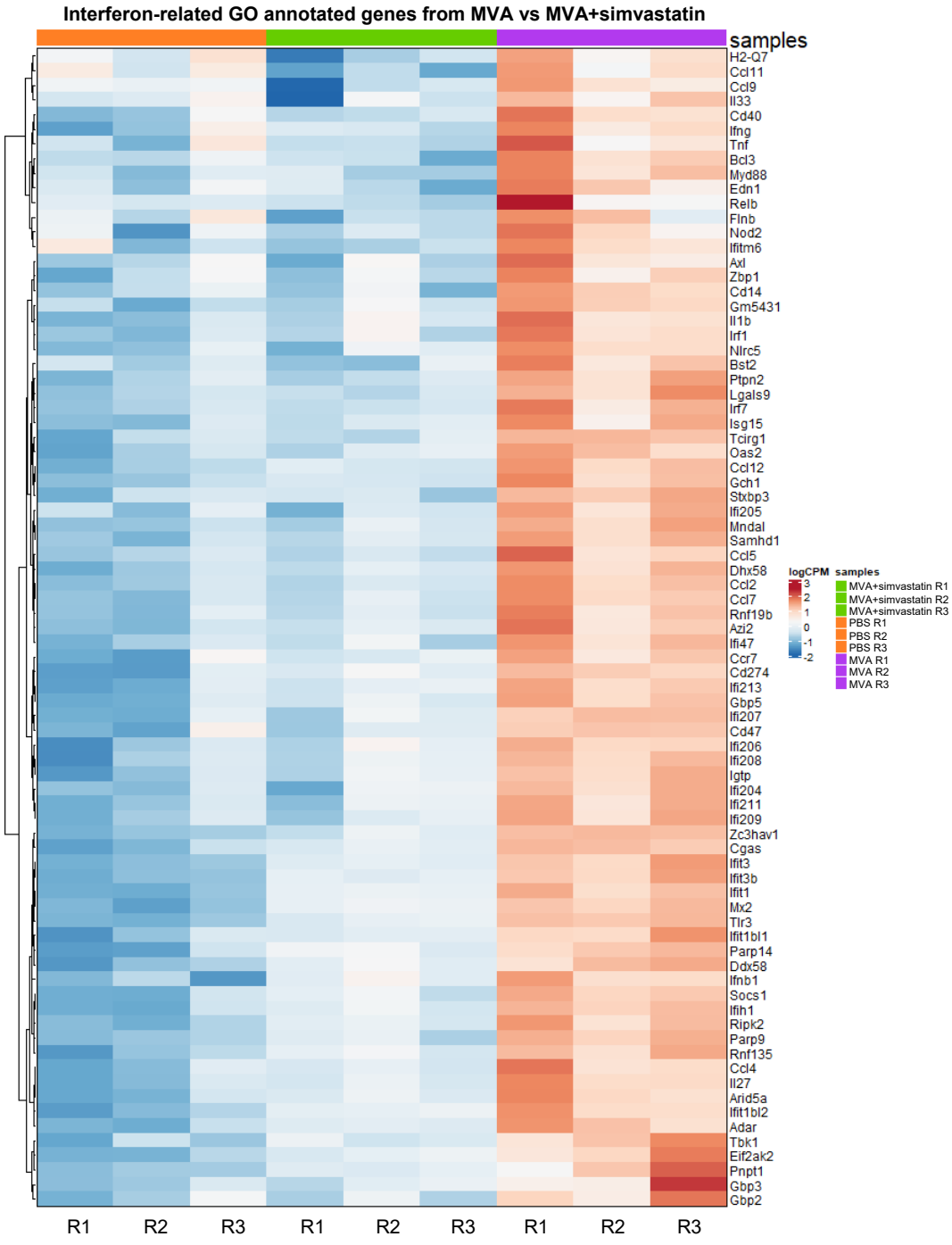
R3

Supplementary Figure 5. Heatmap of cytokine-related GO annotated genes from MVA vs MVA+simvastatin. B16-OVA melanoma cells were injected subcutaneously. Seven days later, mice were treated intraperitoneally (i.p) with vehicle or simvastatin (20 µg/mice). After 2 hours, MVA-OVA ($5x10^7$ TCID50 per mouse) was administered peritumorally (p.t.). Four hours later, mice were sacrificed, and tumor mRNA was analyzed by RNAseq. The heatmap represents the cytokine-related genes differentially expressed between the MVA group and the MVA+simvastatin group.



Supplementary Figure 6. Heatmap of interferon-related GO annotated genes from MVA vs MVA+simvastatin. B16-OVA melanoma cells were injected subcutaneously. Seven days later, mice were treated intraperitoneally (i.p) with vehicle or simvastatin (20

μg/mice). After 2 hours, MVA-OVA ($5x10^7$ TCID50 per mouse) was administered peritumorally (p.t.). Four hours later, mice were sacrificed, and tumor mRNA was analyzed by RNAseq. The heatmap represents the interferon-related genes differentially expressed between the MVA group and the MVA+simvastatin group.

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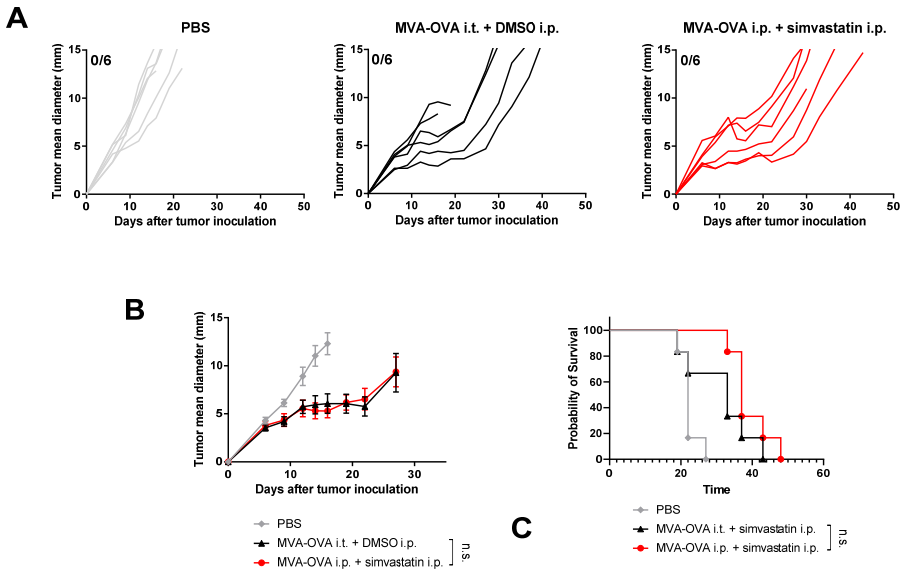
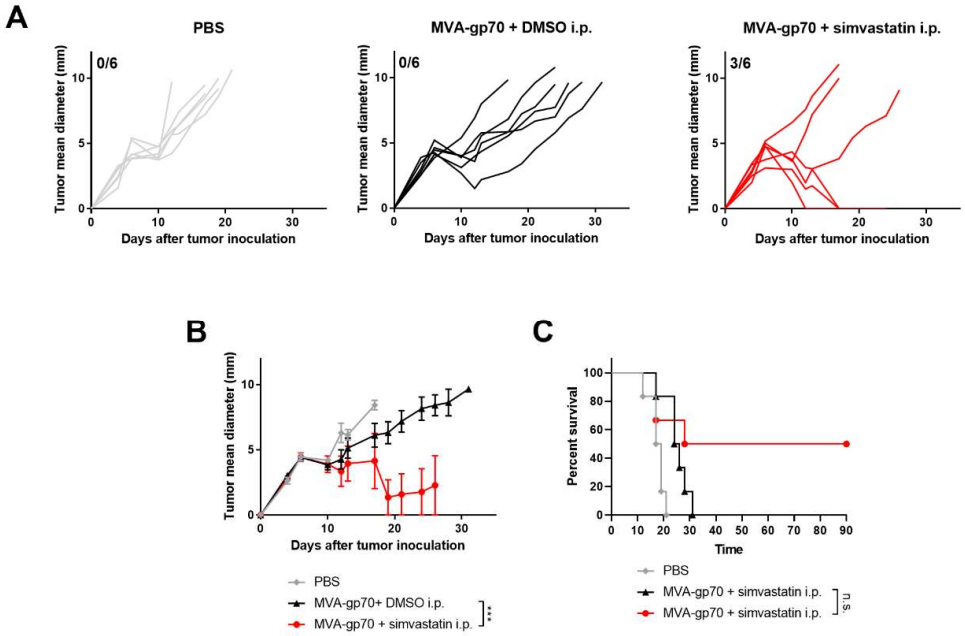
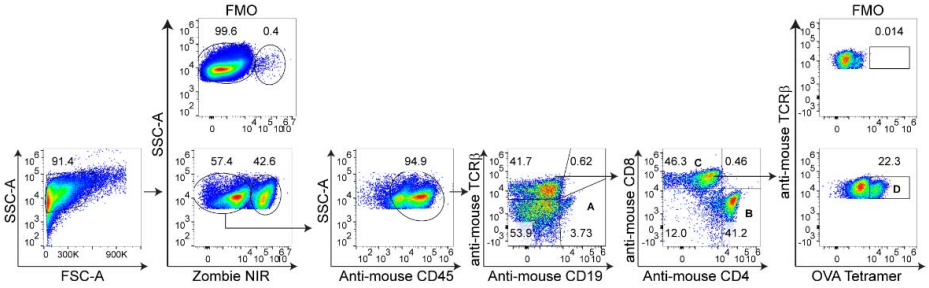


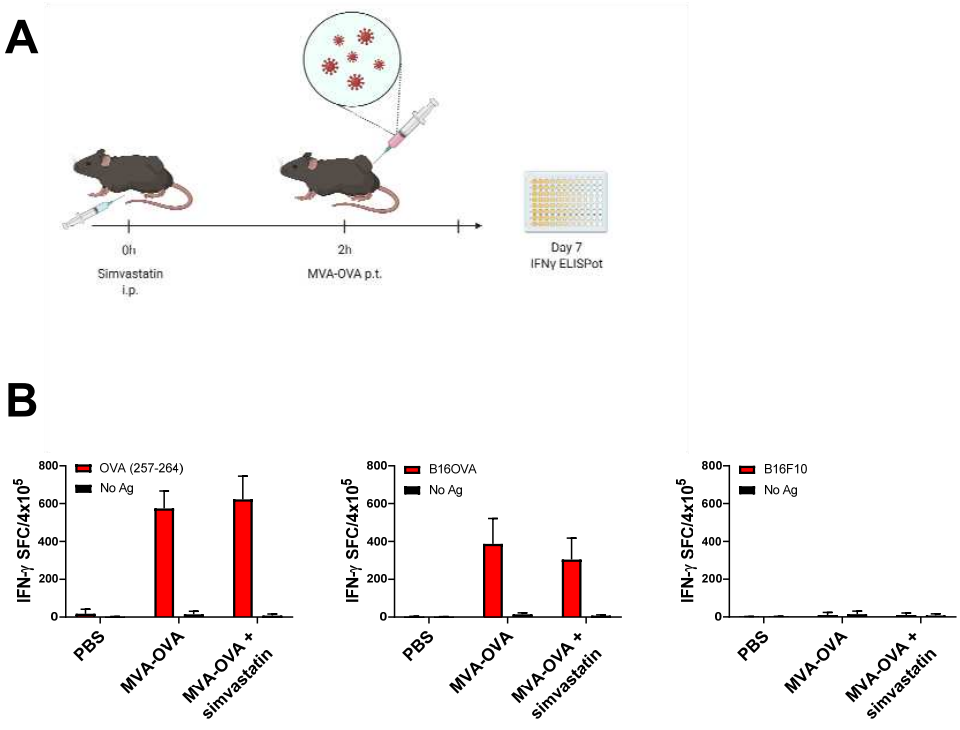
Supplementary Figure 7. Simvastatin does not enhance the antitumor activity of MVA-OVA i.p. B16-OVA melanoma cells were injected subcutaneously. Seven and fourteen days later, mice were treated intraperitoneally with vehicle or simvastatin (20 µg/mice). After 2 hours. MVA-OVA ($5x10^7$ $TCID_{50}$ per mouse) was administered intraperitoneally. A) Individual follow-up of mean tumor diameters indicating the fraction of mice completely rejecting established tumors. N= 6. B) Mean + SEM of different experimental groups. Data were fitted to a third-order polynomial and compared using Extra sum-of-squares F test with Bonferroni correction. n.s $p>0.05$ C) Overall survival of the indicated treatment groups. Log-rank test with Benjamini-Hochberg correction. n.s $p>0.05$.



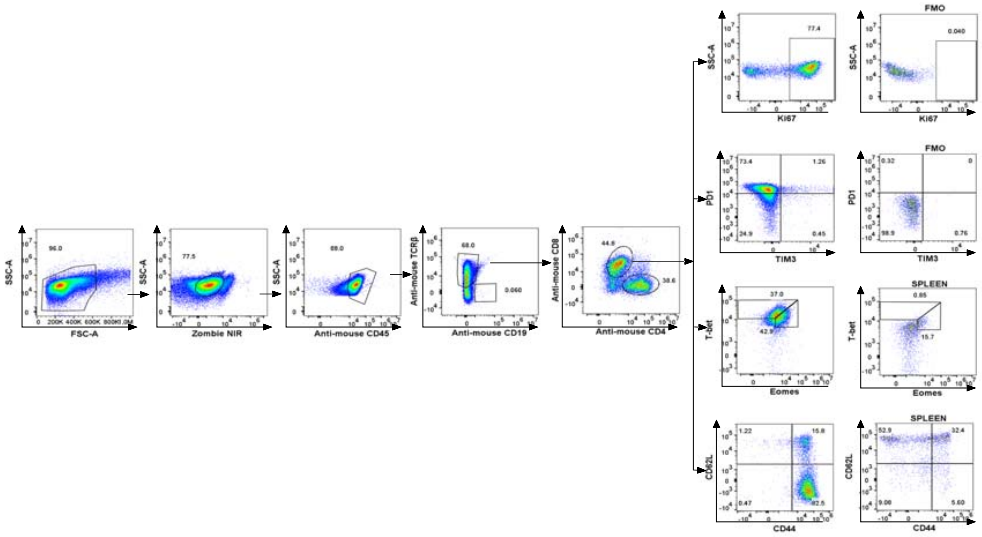
Supplementary Figure 8. Simvastatin enhances the antitumor activity of MVA-gp70 in the LLC-OVA lung cancer model. LLC-OVA lung cancer cells were injected subcutaneously in C57BL/6 mice. Four and eleven days later, mice were treated intraperitoneally with vehicle or simvastatin (20 µg/mice). After 2 hours. MVA-gp70 ($5x10^7$ $TCID_{50}$ per mouse) was administered subcutaneously in the tumor area. A) Individual follow-up of mean tumor diameters indicating the fraction of mice completely rejecting established tumors. N= 6. B) Mean + SEM of different experimental groups. Data were fitted to a third-order polynomial and compared using Extra sum-of-squares F test with Bonferroni correction. *** $p<0.001$ C) Overall survival of the indicated treatment groups. Log-rank test with Benjamini-Hochberg correction. n.s. $p>0.05$.



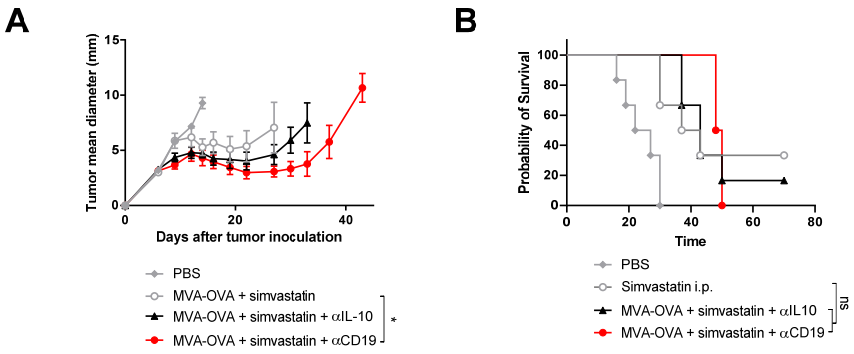
Supplementary Figure 9. Schematic representation of gating strategy followed in figure 5. $CD45^+$ cells were first selected by gating in live scatter and live cells (Zombie NIR^-). (A) CD19 B cells ($CD19^+TCR\beta^-/CD45^+$). (B) CD4 T cells ($CD4^+/CD19^-TCR\beta^+/CD45^+$). (C) CD8 T cells ($CD8^+/CD19^-TCR\beta^+/CD45^+$). (D) Antigen-specific CD8 T cells (OVA $tet^+/CD8^+/CD19^-TCR\beta^+/CD45^+$



Supplementary Figure 10. Simvastatin does not enhance epitope spreading. B16-OVA melanoma cells were injected subcutaneously. Seven days later, mice were treated intraperitoneally with vehicle or simvastatin (20 µg/mice). After 2 hours. MVA-OVA ($5x10^7$ TCID50 per mouse) was administered subcutaneously in the peritumoral area. Seven days after treatment, IFNγ ELISpot assay was performed to determine the $CD8^+$ T lymphocytes against the OVA peptide 257-264, B16-OVA cells or B16F10 cells.



Supplementary Figure 11. Schematic representation of gating strategy followed in Figure 6. $CD45^+$ cells were first selected by gating in live cells (Zombie NIR^-). CD8 T cells ($CD8^+/CD19^-TCR\beta^+/CD45^+$), $CD8^+Ki67^+$ ($Ki67^+/CD8^+/CD19^-TCR\beta^+/CD45^+$), $CD8^+PD\text{-}1^+$ ($PD\text{-}1^+TIM3^-/CD8^+/CD19^-TCR\beta^+/CD45^+$), $CD8^+TIM3^+$ ($TIM3^+PD\text{-}1^-/CD8^+/CD19^-TCR\beta^+/CD45^+$), $CD8^+CD44^+$($CD44^+CD62L^-/CD8^+/CD19^-TCR\beta^+/CD45^+$), CD8+$Eomes^{high}$ T-bet^{dim} ($Eomes^{high}$ T-$bet^{dim}/CD8^+/CD19^-TCR\beta^+/CD45^+$).



Supplementary Figure 12. Effect of monoclonal antibodies against CD19 or IL10 in the antitumor effect of MVA-OVA + simvastatin. B16-OVA melanoma cells were injected subcutaneously. Seven and fourteen days later, mice were treated intraperitoneally with vehicle or simvastatin (20 µg/mice), after 2 hours, MVA-OVA ($5x10^7$ TCID50 per mouse) was administered subcutaneously in the tumor area. Anti-CD19 mAb (500 µg/mice) was administered intra-peritoneally one day before first therapeutic treatment administration and on days +2, +7, +12, +17, +22 and +27. Anti-IL10 mAb (250 µg/mice) was administered intra-peritoneally after the first therapeutic treatment administration and on days +7, and +14. A) Mean +SEM of the different experimental groups. Data were fitted to a third-order polynomial and compared using Extra sum-of-squares F test with Bonferroni correction. * $p<0.05$ B) Overall survival of the indicated treatment groups. Log-rank test with Benjamini-Hochberg correction. n.s $p>0.05$.