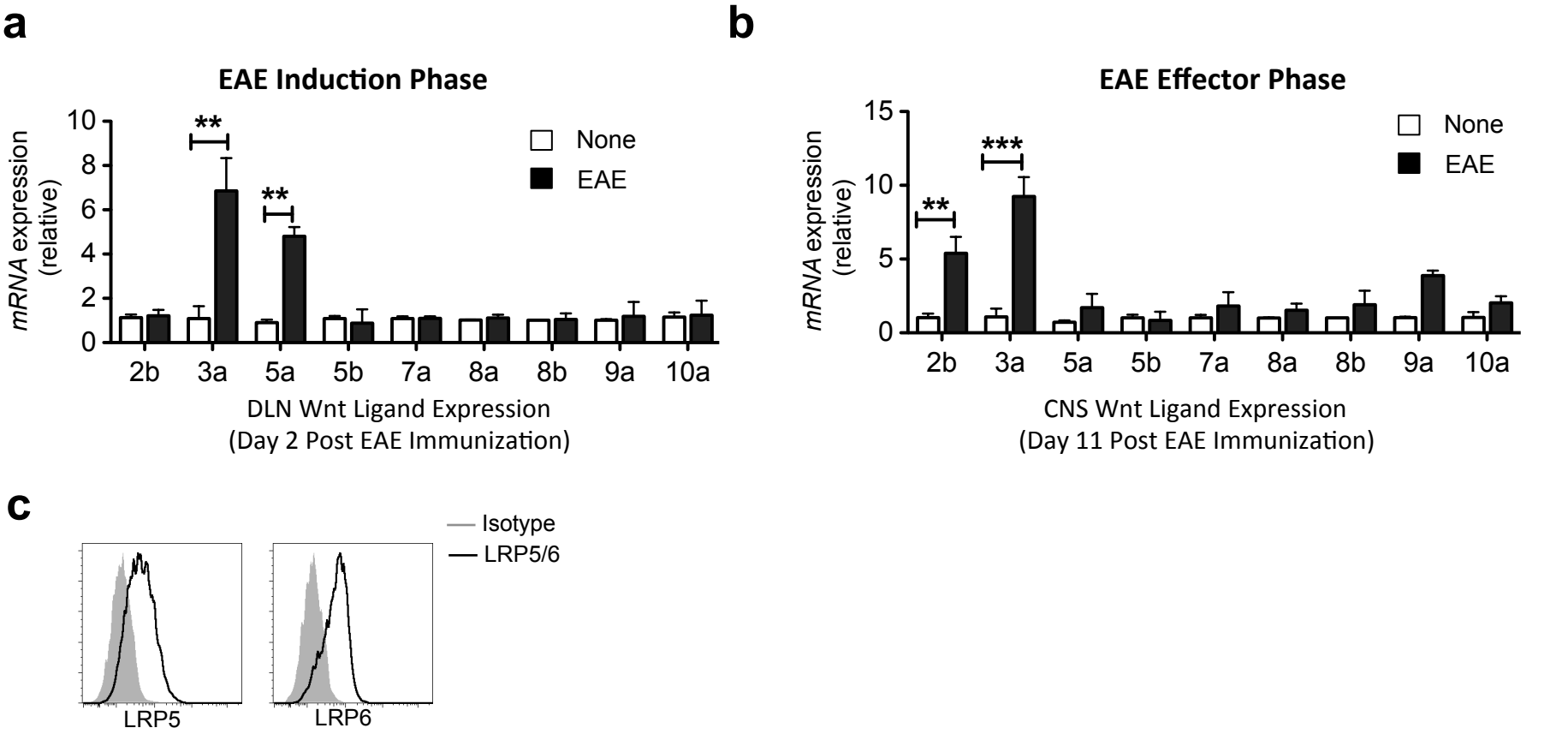
Supplementary Figure 1



Supplementary Figure 1. DCs express both wnt co-receptors LRP5 and LRP6. $WT^{FL/FL}$ mice were immunized with 100 µg MOG_{35-55} in CFA on day 0. Mice also received 250 ng of pertussis toxin on days 0 and 2 pi. Quantitative real-time PCR analysis shows relative fold expression in various wnt ligands in the DLN **(a)** on day 2 pi (induction phase) and brain**(b)** on day 11 pi (effector phase) compared to control (No EAE) mice. **(c)** Representative histograms of surface expression levels of LRP5 and LRP6 in $CD11c^+$ splenic DCs. Data are representative of at least two experiments (a-b, n= DLN and CNS pooled from 5 mice per experiment values represented in triplicates; d, n=3). Error bars show mean values ± SEM. $^{**}p<0.001$; $^{***}p<0.0001$.

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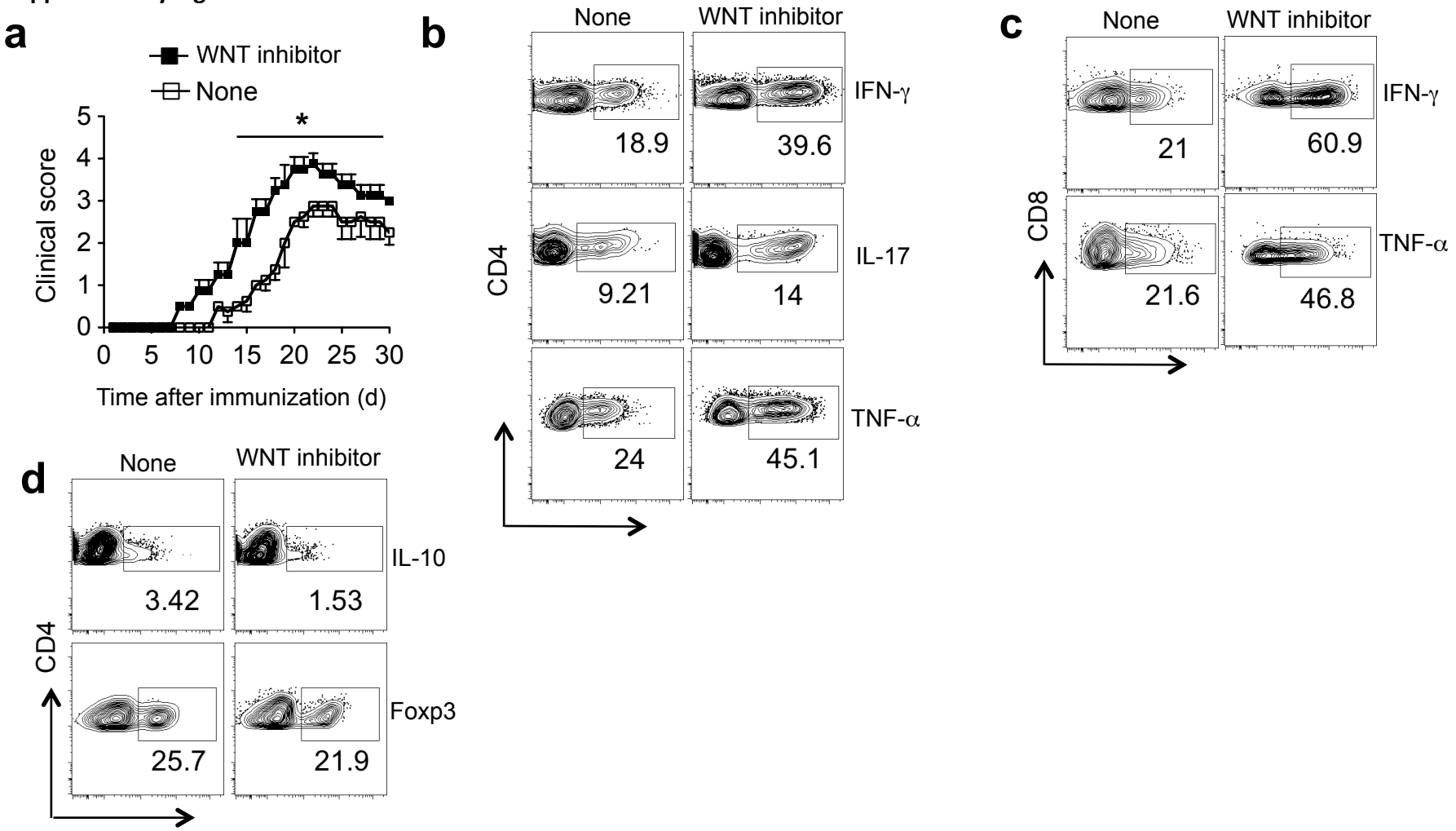
Supplementary Figure 2.



Supplementary Figure 2. Inhibition of wnt-mediated signaling during EAE exacerbates EAE pathology. (a) EAE-induced WT mice were treated with Wnt inhibitor (5 mg/kg) or left untreated/control vehicle (PBS) (none) on day 0, 3 and 5 pi. The EAE disease progression was monitored in control and wnt inhibitor-treated groups over 30 days pi. Mean clinical EAE score in no treatment (None) and wnt inhibitor-treated mice. **(b)** Representative FACS plots for IFN-γ (top panels), IL-17A (middle panels), and TNF-α (Bottom panels)-producing $CD4^+$ T cells or **(c)** IFN-γ (top panels) and TNF-α (Bottom panels)-producing $CD8^+$ T cells isolated from the CNS of control and wnt inhibitor-treated mice on day 16 pi. The cells were stimulated with PMA/ionomycin for 6 h in the presence of brefeldin A and monensin followed by ICS. **(d)** Representative FACS plot for IL-10^+ (top panels) and $Foxp3^+$ (bottom panels) $CD4^+$ T cells isolated from the CNS of control and wnt inhibitor-treated mice on day 16 pi. Data are representative of two (a), three (b-d) experiments (a, n= 4 to 5 mice per group per experiment; b-d, n= representative of 3 mice per experiment). Error bars show mean values ± SEM. *p<0.01.

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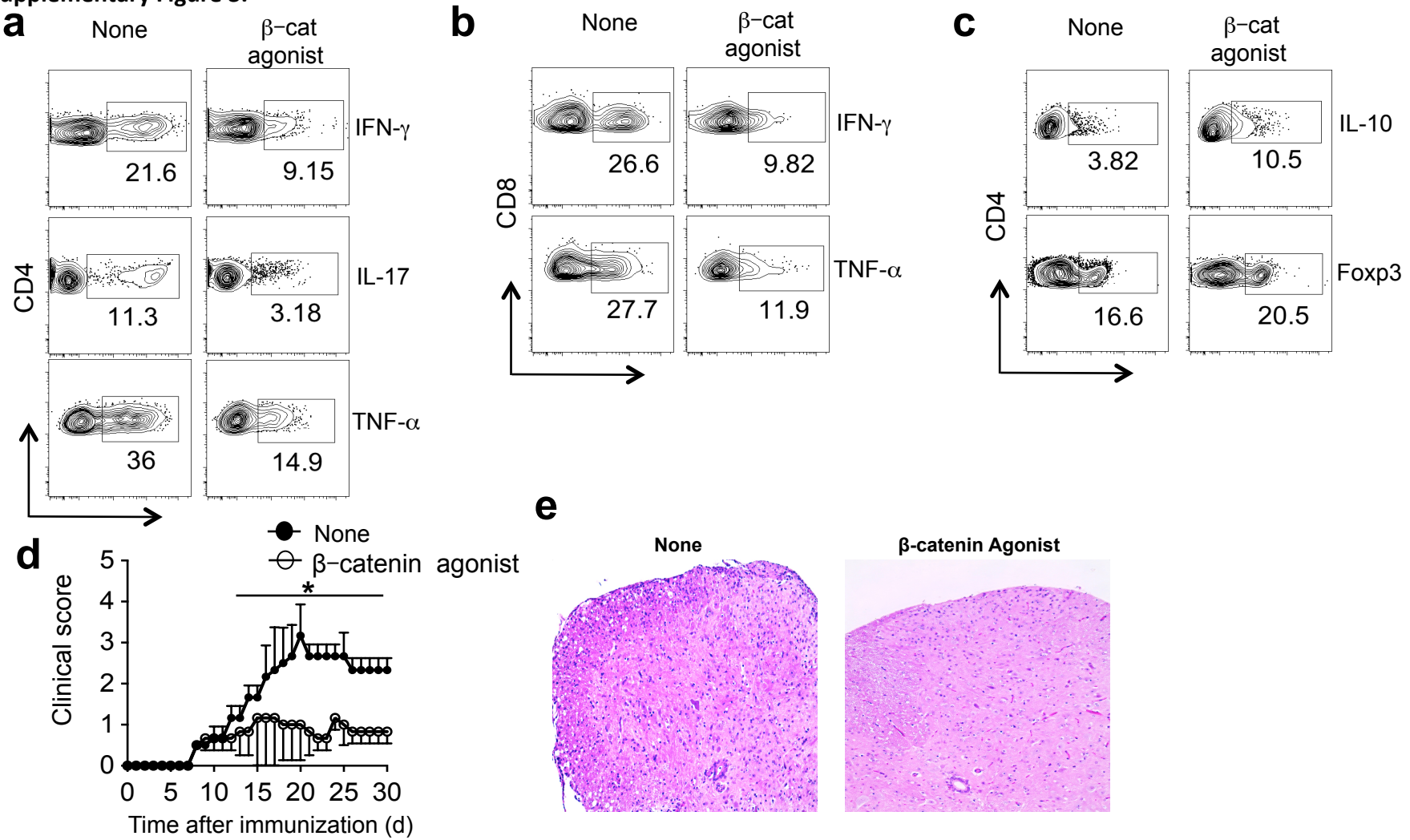
Supplementary Figure 3.



Supplementary Figure 3. Pharmacological activation of the wnt/β-catenin pathway during EAE differentially regulates regulatory and effector T cell populations in the CNS. Representative FACS plots for IFN-γ (top panels), IL-17A (middle panels), and TNF-α (Bottom panels)-producing $CD4^+$ T cells **(a)** or IFN-γ (top panels) and TNF-α (Bottom panels)-producing $CD8^+$ T cells **(b)** isolated from the CNS of control and β-catenin agonist (5 mg/kg)-treated mice on day 16 pi. The cells were stimulated with PMA/ionomycin for 6 h in the presence of brefeldin A and monensin followed by intracellular cytokine staining (ICS). **(c)** Representative FACS plot for IL-10^+ (top panels) and Foxp3 (bottom panels)-expressing $CD4^+$ T cells isolated from the CNS of control and β-catenin agonist-treated mice on day 16 pi. Data are representative of two experiments; n= representative FACS plot of 3 per experiment. **(d)** EAE-induced WT mice were treated with β-catenin agonist (5 mg/kg) or left untreated/control vehicle (PBS) (None) on day 10, 13 and 16 pi. The EAE disease progression was monitored in control and β-cat agonist treated groups over 30 days pi. Mean clinical EAE score with no treatment (None) and β-catenin agonist treated mice. **(e)** H&E staining of spinal cords of none and β-catenin agonist treated mice representative of mean EAE scores on day 30 pi. Original magnification, 20X.

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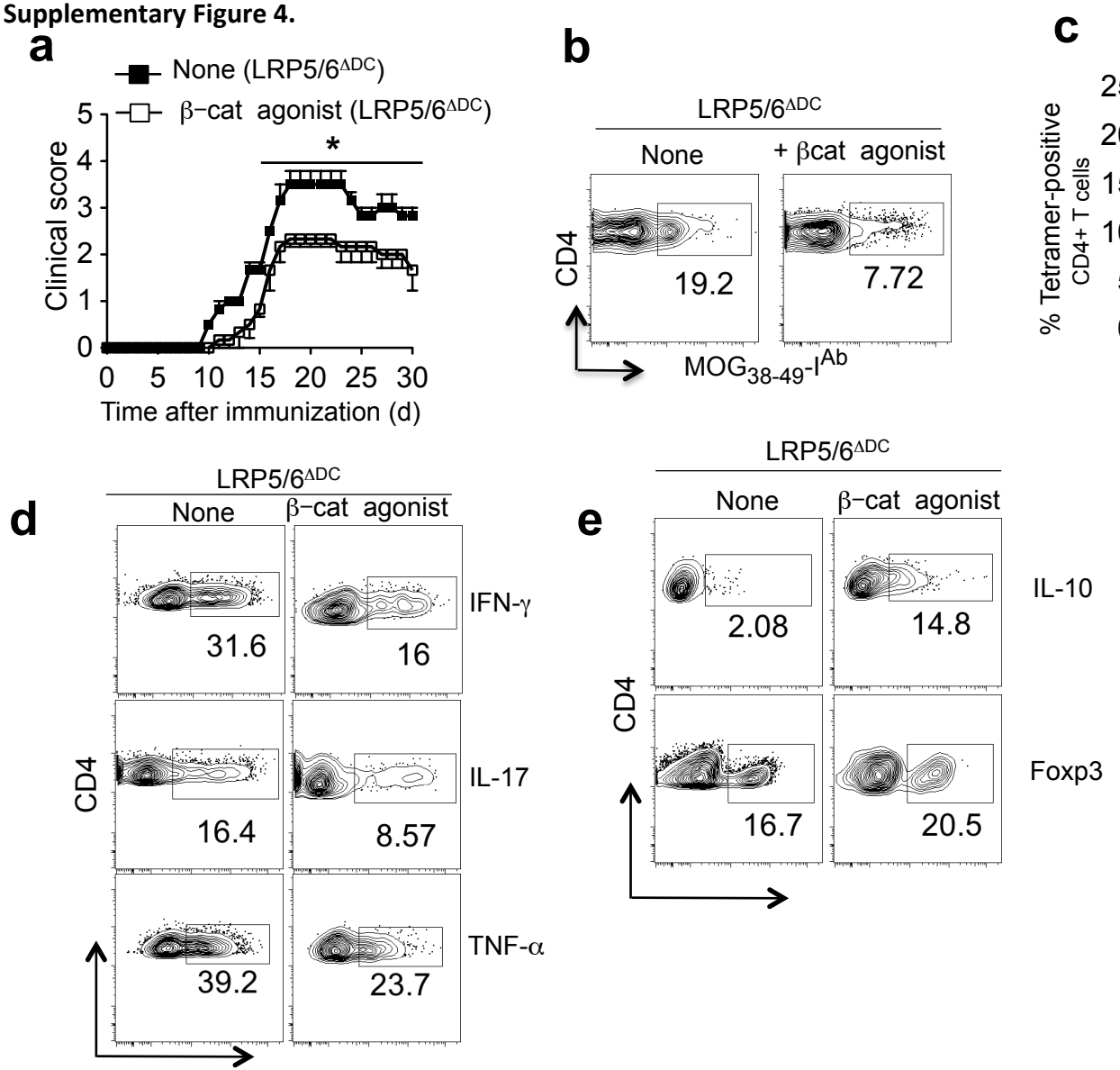
Supplementary Figure 4.



Supplementary Figure 4. Activation of β-catenin using β-catenin agonist in LRP5/6$^{\Delta DC}$ mice suppresses severe EAE pathology. (a) The progression of EAE disease course in LRP5/6$^{\Delta DC}$ mice and β-catenin agonist (5 mg/kg)-treated LRP5/6$^{\Delta DC}$ mice immunized with MOG_{35-55} plus CFA. Mean clinical EAE score in LRP5/6$^{\Delta DC}$ mice and β-catenin agonist-treated LRP5/6$^{\Delta DC}$. **(b)** Representative FACS plot and **(c)** bar diagram for the frequency of MOG_{35-55} tetramer-specific CD4$^+$ T cells isolated from the CNS of LRP5/6$^{\Delta DC}$ mice and β-catenin agonist-treated LRP5/6$^{\Delta DC}$ mice on day 16 pi. Representative FACS plots of IFN-γ$^+$, IL-17$^+$, and TNF-α$^+$-producing CD4$^+$ T cells **(d)**, and IL-10 and Foxp3-expressing CD4$^+$ T cells **(e)** isolated from LRP5/6$^{\Delta DC}$ mice and β-catenin agonist-treated LRP5/6$^{\Delta DC}$ mice CNS on day 16 pi. Data are representative of at least two experiments (a, n= 4 to 5 mice per group per experiment; b-c, n=3; d-e, n=3). Error bars show mean values ± SEM. *p<0.01; **p<0.001.

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