

**Supplementary Figure 1** 

**Sup. Figure 1: A)** Carlr levels in the mouse intestinal cells in basal conditions and after LPS stimulation. Data represents the average and standard error of three independent experiments. **B)** Circular plot of genes analyzed as potential Carlr targets, clustered by expression pattern after LPS stimulation (each clustered labeled with a different color dot). Fold change values retrieved from the STEM (short term expression miner) software(18). R-values represent the correlation between Carlr expression and each of the target genes and are represented as red dots; darker corresponds to higher correlation. Outer expression plot corresponds to 2h stimulation; inner expression plot corresponds to 16h stimulation. **C)** Decrease in phosphorylated lkBa in the cytoplasm of sh1 and sh2 cell lines.  $\beta$ -tubulin and Hdac1 were used as loading controls of the fractions.



**Sup. Figure 2: A)** RNAseq data of the corresponding human Carlr region in different human tissues. Data retrieved from the Epigenome Roadmap project. **B)** RT-qPCR of the Carlr region in different human tissues. Conserved region 1 is outside (5' side) the corresponding mouse coding region, while conserved region 2 lays into the coding conserved region. **C)** Expression of Carlr in the human monocytic cell line U937 in basal conditions and after LPS stimulation. + p<0.1. Data represents the mean and standard error of three quantifications. **D)** Carlr localization in U937 cell line, represented as average and standard error of two independent fractionations.



**Sup. Figure 3: A)** Carlr levels are significantly reduced in both si3 and si5 transduced cell lines. siCTRL was used as a control. Data represents the mean and standard error of three independent experiments. \*\*p<0.01, \*p<0.05. **B**) ImageJ quantification of the p50 and p65 NFKB subunits in the cell nucleus of the Caco2 cells after different conditions. Amounts were normalized to Hdac1 signal. Data represents the average and standard error of three independent blots. +p=0.1, \*p<0.05, paired t-test. **C)** Quantitative expression of human Carlr in small intestinal biopsies of control and CeD patients. p = 0.018; unpaired t-test. White circles show the medians; box limits indicate the 25th and 75th percentiles as determined by R software; whiskers extend 1.5 times the interquartile range from the 25th and 75th percentiles; polygons represent density estimates of data and extend to extreme values. **D)** Co-IP of IkBa in control and CeD samples showing interaction with NF-kB in the control samples only. Representative WB of three pairs of samples (left). Carlr quantification after IkBa RIP (right).