**Supplemental materials**

**Cell culture**

Cells were cultured in RPMI1640 medium. The medium was supplemented with glutamine (2 mM), fetal calf serum (10%), penicillin (100 U/ml) and streptomycin (0.1 mg/ml). Cell viability was greater than 99% as assessed by Trypan blue exclusion assay.

**Flow cytometry**

Single cells were prepared and stained with fluorescence-labeled antibodies of interest (see figures for antibody types) or isotype IgG on ice for 30 min. After washing with phosphate buffered saline (PBS), cells were analyzed with a flow cytometer (FACSCanto II, BD Bioscience). In the intracellular staining, cells were fixed by 1% paraformaldehyde (containing 0.05% Triton X-100 to increase the cell membrane permeability) prior to antibody staining. The data were analyzed with a software package, FlowJo (Tree Star Inc., Oakland, OR); the data obtained from isotype IgG staining were used as gating references.

**Real-time quantitative RT-PCR (RT-qPCR)**

Total RNAs were extracted from cells collected from relevant experiments. The RNAs were converted to cDNA with a reverse transcription kit following the manufacturer’s instruction. The cDNA was amplified in a qPCR device (The CFX96 Touch System) with SYBR Green Master Mix and the presence of primers of CD83 (gctctcctatgcagtgtcct and actctgtagcttccttgggg) or TIEG1 (catccgtcacacagctgatg and tgtctctgaggaaggcacag). The results were processed by the 2-∆∆ Ct method and presented as relative quantification (RQ).

**Protein extraction**

Cells were collected from relevant experiments and lysed with lysis buffer (10 mM HEPES; 1.5 mM MgCl2; 10 mM KCl; 0.5 mM DTT; 1 mM EDTA; 0.05% NP40 and protease inhibitor cocktail). The lysates were centrifuged at 13,000 *g* for 10 min. Supernatant was collected and used as the cytosolic proteins. The pellets were resuspended in nuclear lysis buffer (5 mM HEPES; 1.5 mM MgCl2SO4; 4.6 M NaCl; 0.2 mM EDTA; 0.5 mM DTT; 26% glycerol) and incubated for 30 min. The lysates were centrifuged at 13,000 *g* for 10 min. Supernatant was collected and used as the nuclear proteins. All procedures were carried out at 4 °C.

**Western blotting**

The proteins were fractioned by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and transferred onto a PVDF (polyvinylidene fluoride) membrane. The membrane was incubated with 5% skim milk for 30 min to block non-specific binding, and then, incubated with primary antibodies (see figures for antibody types) of interest (diluted in 1:300) overnight at 4 °C, washed with Tris-buffered saline containing 0.05% Tween 20 (TBST) 3 times, incubated with peroxidase-labeled secondary antibodies (diluted in 1:5000) for 2 h at room temperature, washed with TBST 3 times. Immunoblots on membrane were developed with the enhanced chemiluminescence and photographed in an imaging device.

**Co-immunoprecipitation (Co-IP)**

The co-IP assay was performed to detect the CD83/TLR4/MD-2 complexes in CD4+ T cells with a reagent kit following the manufacturer’s instruction. Briefly, proteins were extracted from CD4+ T cells and incubated with protein G sepharose beads to clear the pre-existing immune complexes. The beads were removed from the samples by centrifugation (3,000 *g*, 5 min). Supernatant was incubated with antibodies against CD83 and TLR4/MD-2 complex overnight. Immunocomplexes in samples were precipitated by incubating with protein G sepharose beads for 2 h. The beads were collected by centrifugation (3,000 *g*, 5 min). Proteins on the beads were eluted and analyzed by Western blotting with anti-CD83 and anti-TLR4/MD-2 complex antibodies to blot the targeted proteins. All the procedures were carried out at 4 °C.

**Immunohistochemistry to illustrate Tregs in the intestinal tissues**

Small intestinal segments were excised upon the sacrifice. The samples were snap frozen with liquid nitrogen. Cryosections were prepared, dried overnight at room temperature and fixed with cold acetone for 20 min. The sections were blocked with 1% bovine serum albumin (BSA) for 30 min, incubated with a primary antibody against Foxp3 (diluted in 1:100) overnight at 4 °C, washed with PBS 3 times, incubated with FITC-labeled secondary antibody for 2 h at room temperature, stained with propidium iodide (PI) to visualize the nuclei, washed with PBS 3 times, mounted with cover slips and observed with a fluorescence microscope. Tregs were counted in 20 randomly selected micro windows per sample (the average of 20 counts was used as one datum). Sections were coded; observers were not aware of the code to avoid observer bias.

**Assessment of Treg immune suppressive effects**

CD4+ CD25¯ T cells (Teff) were isolated from the DO11.10 mouse spleen, labeled with carboxy fluorescein succinimidyl ester (CFSE) and cultured (105 cells/ml) with inducible OVA-specific Tregs (CD4+ CD25+ CD127¯; 105 cells/ml) in the presence of DC (2×104 cells/ml) and OVA (20 µg/ml) for 3 days. Tregs isolated from naive BALB/c mice were used as control Tregs. The cells were analyzed by flow cytometry, the CFSE-dilution assay. The Teff proliferation changes were used as an indicator of the Tregs’ immune suppressive effects.

**Generation of mice with *CD83*-deficient epithelial cells (CD83d mice) and mice with TIEG1-deficient CD4+ T cells (TIEG1d mice)**

The *CD83* gene in epithelial cells or the *TIEG1* gene in CD4+ T cells were specifically knocked out in C57BL/6 mice via the genetic engineering technique. To maintain the role of CD83 or TIEG1 in other cells, the *CD83* gene was specifically depleted from epithelial cells with EpCAM as the specific cell marker or the *TIEG1* gene was specifically depleted from CD4+ T cells with CD4 as the specific marker. Referring previous reports (Elife 2014; 3: e01949; J Clin Invest 1996; 98: 600-3), mice with loxP-flanked *CD83* gene (flox) or loxP-flanked TIEG1 gene (flox) were developed. In both cases, a gene targeting vector containing 3 loxP sites was constructed, of which 2 of them flanking the neomycin resistance gene. The genomic locus was modified between vector and the *CD83* gene (or the *TIEG1* gene) in embryo stem (ES) cells by homologous recombination approach. The loxP-flanked *CD83* gene (or the *TIEG1* gene) was targeted by EpCAM-Cre expression (or CD4-Cre expression) in ES cells (EpCAM is specifically expressed in epithelial cells, including airway epithelial cells; refer to: Respir Res. 2017; 18: 150). Employing the modified ES cells, a mouse line containing loxp-*CD83* (or the *TIEG1* gene) was generated. Then, the mouse strain harboring two loxP sites in the *CD83* gene (or the *TIEG1* gene) was crossed with another mouse strain expressing EpCAM-Cre recombinase (expressing CD4-Cre recombinase). Thus, only in cells expressing EpCAM-Cre the *CD83* gene becomes inactivated and in cells expressing CD4-Cre the *TIEG1* gene becomes inactivated, the *CD83* gene (or the *TIEG1* gene) remained active in other cells of the body. To keep the *CD83* gene (or the *TIEG1* gene) active until the experimental period, the Cre gene was modified to be functional only in the ribosomes, but could not penetrate into the nuclei. Thus, the loxp-*CD83* gene (or the *TIEG1* gene) was remained intact in the mice. One week prior to the experiments, the mice were fed with tamoxifen citrate salt (Sigma Aldrich, St. Louis, MO; 0.3 g/kg in 0.2 ml 10% Etoh in corn oil) daily for 5 consecutive days. Control mice received oral gavage of 0.2 ml 10% EtoH in oil. Tamoxifen increases the permeability of the nuclear membrane to allow the EpCAM-Cre or CD4-Cre penetrate the nuclei to cleave the flox-*CD83* gene or the flox-*TIEG1* gene. As assessed by RT-qPCR and Western blotting, all EpCAM+ epithelial cells in the intestinal tissues did not express CD83 and all CD4+ T cells in the intestinal tissues did not express TIEG1 (Fig. S5-S6).



**Figure S1. Phenotypes of CD83+ cells in LPMCs**. Small intestinal tissues were sampled from normal control (NC) mice (n=10) and food allergy (FA) mice (n=10). Single cells were prepared with the samples and analyzed by flow cytometry. The CD83+ cells were gated into epithelial cells (EpCAM+ cells) and non-epithelial cells (refer to Fig. 1). The flow cytometry plots and bar graphs show CD83+ CD4+ T cells (A, B), CD83+ B cells (C, D), CD83+ DCs (E, F), CD83+ macrophages (G, H), CD83+ eosinophils (I, J) and CD83+ mast cells (K, L) in the non-epithelial CD83+ cells. The data of bars are presented as mean ± SEM of 10 mice per group. Each sample was analyzed in triplicate. Statistics: The Student’s *t*-test.



**Figure S6. Depletion of the CD83 expression in IECs**. A, single cells were prepared with the intestinal tissues obtained from mice carrying CD83-deficient epithelial cells and analyzed by flow cytometry. The gated plots show CD83+ IEC counts in the single cells. B, IECs were isolated from the intestinal tissues and analyzed by Western blotting. The immunoblots show CD83 proteins in purified IECs.



**Figure S3. Depletion of TLR4 in CD4+ T cells**. DO11.10 CD4+ T cells were isolated from the mouse spleen and treated with a CRISPR reagent kit following the manufacturer’s instructions. Cells were harvested 48 h after and analyzed by flow cytometry and Western blotting. A, the gated plots show TLR4+ CD4+ T cell counts. B, the immunoblots show TLR4 protein levels in CD4+ T cell protein extracts. The data represent 3 independent experiments. Each sample was analyzed in triplicate.



**Figure S4.** **Depletion of MD-2 in CD4+ T cells**. DO11.10 CD4+ T cells were isolated from the mouse spleen and treated with a CRISPR reagent kit following the manufacturer’s instructions. Cells were harvested 48 h after and analyzed by flow cytometry and Western blotting. A, the gated plots show MD-2+ CD4+ T cell counts. B, the immunoblots show MD-2 protein levels in CD4+ T cell protein extracts. The data represent 3 independent experiments. Each sample was analyzed in triplicate.



**Figure S5.** **Depletion of TIEG1 in CD4+ T cells**. DO11.10 CD4+ T cells were isolated from the mouse spleen and treated with a CRISPR reagent kit following the manufacturer’s instructions. Cells were harvested 48 h after and analyzed by flow cytometry and Western blotting. A, the gated plots show TIEG1+ CD4+ T cell counts. B, the immunoblots show TIEG1 protein levels in CD4+ T cell protein extracts. The data represent 3 independent experiments. Each sample was analyzed in triplicate.



**Figure S6. Depletion of the TIEG1 expression in CD4+ T cells**. A, lamina propria mononuclear cells (LPMC) were isolated from the intestinal tissues of mice carrying the TIEG1-deficient CD4+ T cells and analyzed by flow cytometry. The gated plots show TIEG1+ CD4+ T cell counts in LPMCs. B, CD4+ T cells were isolated from the intestinal tissues and analyzed by Western blotting. The immunoblots show TIEG1 proteins in purified CD4+ T cells.



**Figure S7. Concomitant administration of CD83 and OVA induces Treg differentiation in the intestine**.

An FA BALB/c mouse model was developed with OVA as the specific antigen. Mice were treated with the procedures denoted above each subpanel. NC: Naive control mice. FA: Food allergy mice. OVA or CD83: Mice were fed with OVA or/and CD83. TIEG1d: Mice with TIEG1-deficient CD4+ T cells. PC61 or isotype IgG: Anti-CD25 Ab (Control Ab): Mice were treated with anti-CD25 Ab or isotype IgG. A, gated plots show Treg counts in LPMCs. B, bars show means ± SEM of 6 mice per group. \*, p<0.01 (ANOVA followed by the Dunnett’s test), compared with the FA group treated with OVA alone.