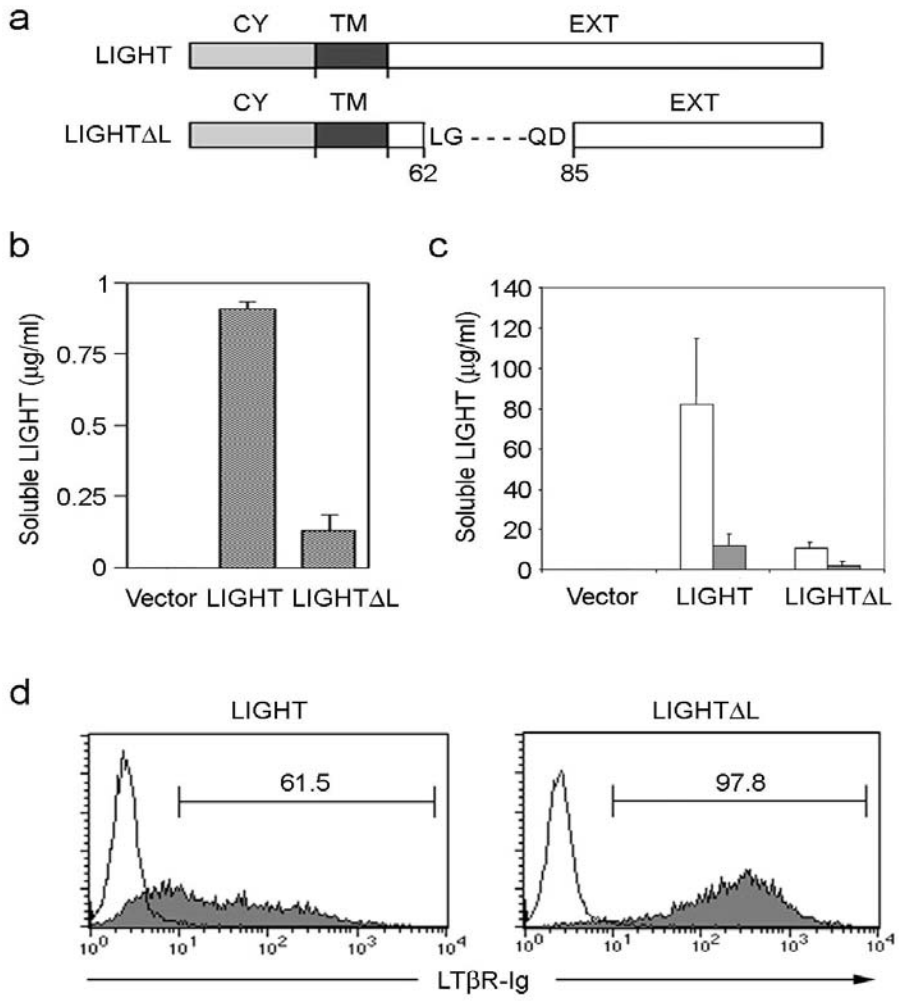
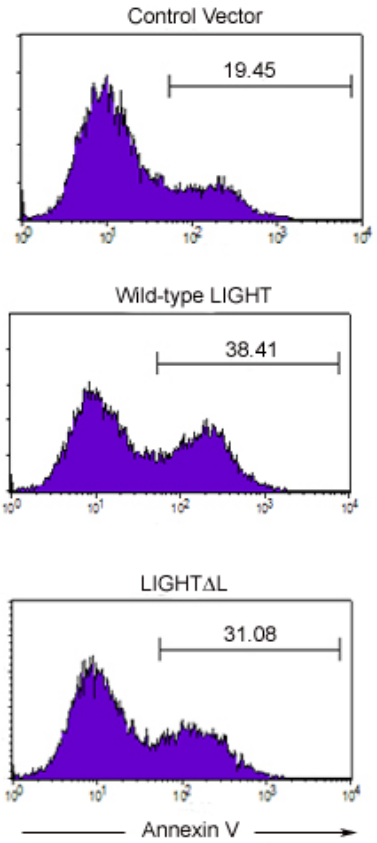


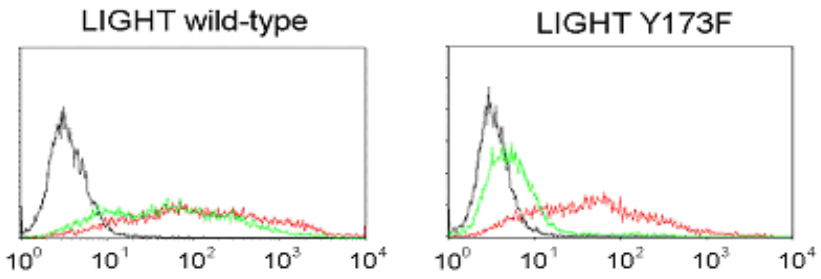
Supplementary Figure 1. Generation of LIGHT mutant resistant to the enzymatic cleavage

(**a**) Structure of wild-type LIGHT and LIGHTΔL is schematically shown. CY, TM and EXT represent the cytoplasmic, transmembrane and extracellular domains, respectively. Amino acid sequences of deleted regions are partially shown. (**b**) 293T cells were transfected with plasmids encoding either control pcDNA3.1, wild-type LIGHT, or LIGHTΔL. After 48 hr, amount of soluble LIGHT in the supernatants was measured by LIGHT-specific ELISA. (**c**) B6 mice were administered with 20 μg plasmid encoding control pcDNA3.1, wild-type LIGHT, or LIGHTΔL using hydrodynamic tail vein injection. Mouse sera were collected 18 hrs (open bar) and 48 hrs (gray bar) later, and assayed for soluble LIGHT concentration by ELISA. (**d**) 293T cells were transfected with plasmids encoding wild-type LIGHT or LIGHTΔL. After 48 hr, the cells were stained with mouse LTβR-human Ig fusion protein (filled line) or control human IgG (open line), followed by FITC-conjugated anti-human IgG. Numbers in histograms represent the percentage of positively stained cells.



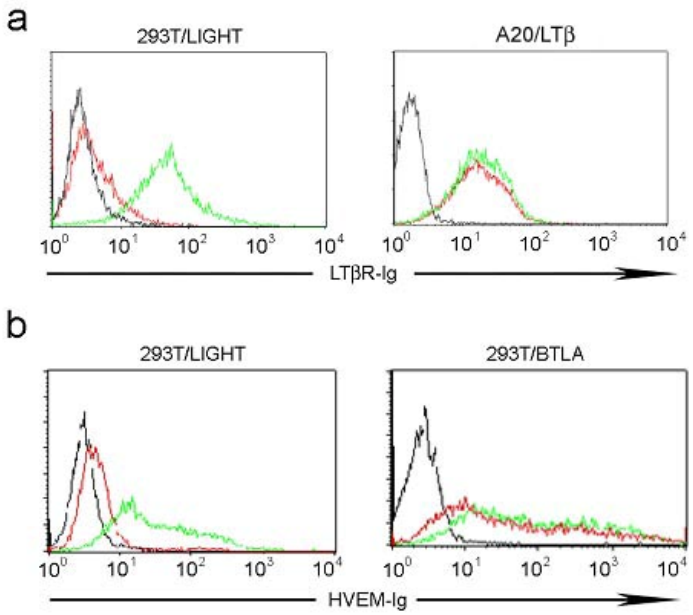
Supplementary Figure 2. Deletion mutant of LIGHT is capable of mediating cell death.

HT-29 cells were co-cultured with GFP-positive 293T cells transiently transfected with either control vector or wild-type LIGHT or LIGHTΔL, in the presence of 50 IU/ml of recombinant human IFN-γ (Ratio of HT29:293T was 1:5). After 3 days, apoptosis of HT-29 cells, gated as GFP-negative population, was assessed by staining with PE-conjugated Annexin V according to the manufacturer's instructions. The numbers indicate the percentage of Annexin V-positive population among HT-29 cells. Data is representative of two independent experiments.



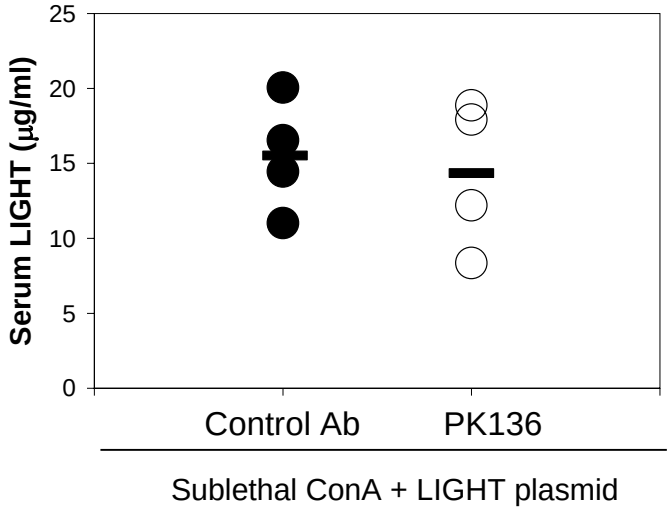
Supplementary Figure 3. LIGHT Y173F mutant loses binding to HVEM while retaining binding to LTβR

293T cells transfected with plasmids encoding wild-type mouse LIGHT (left panel) or LIGHT Y173F mutant (right panel) were stained with biotin-conjugated control Ig (black), HVEM-Ig (green), or LTβR-Ig (red), followed by streptavidin-PE. LIGHT Y173F selectively loses binding affinity to HVEM.



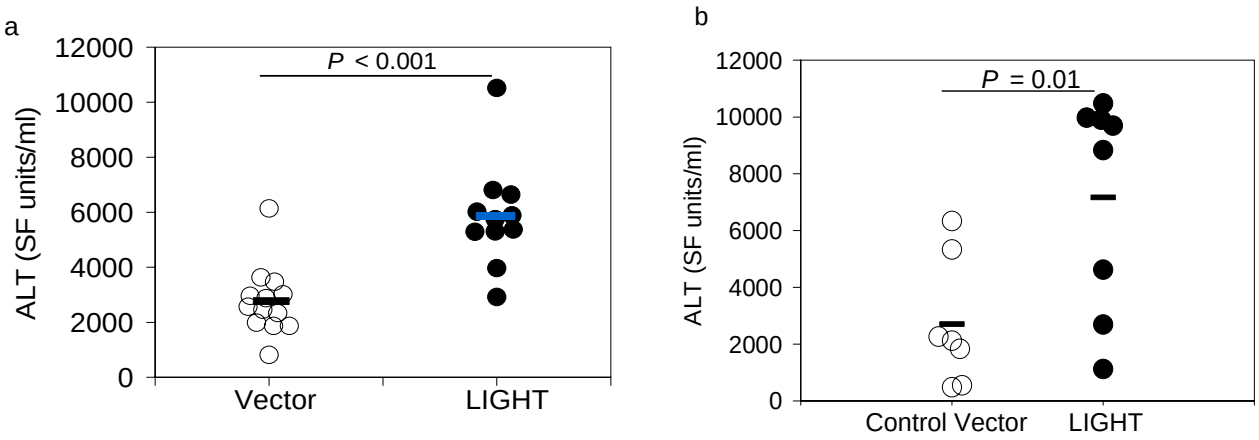
Supplementary Figure 4. Characterization of antagonistic mAbs against LTβR and HVEM

(**a**) 293T cells transfected with mouse LIGHT plasmid (left panel) or activated A20 cells expressing LTβ (right panel) were stained with 2 μg of control Ig-biotin (black), LTβR-Ig-biotin (green), or LTβR-Ig-biotin pre-incubated with 20 μg of anti-LTβR mAb for 30 min (red). Staining intensity was detected by PE-conjugated streptavidin. (**b**) 293T cells transfected with either mouse LIGHT (left panel) or BTLA (right panel) plasmid were stained with 2 μg of control Ig-biotin (black), HVEM-Ig-biotin (green), or HVEM-Ig-biotin pre-incubated with 20 μg of anti-HVEM mAb for 30 min (red). Staining intensity was detected by PE-conjugated streptavidin.



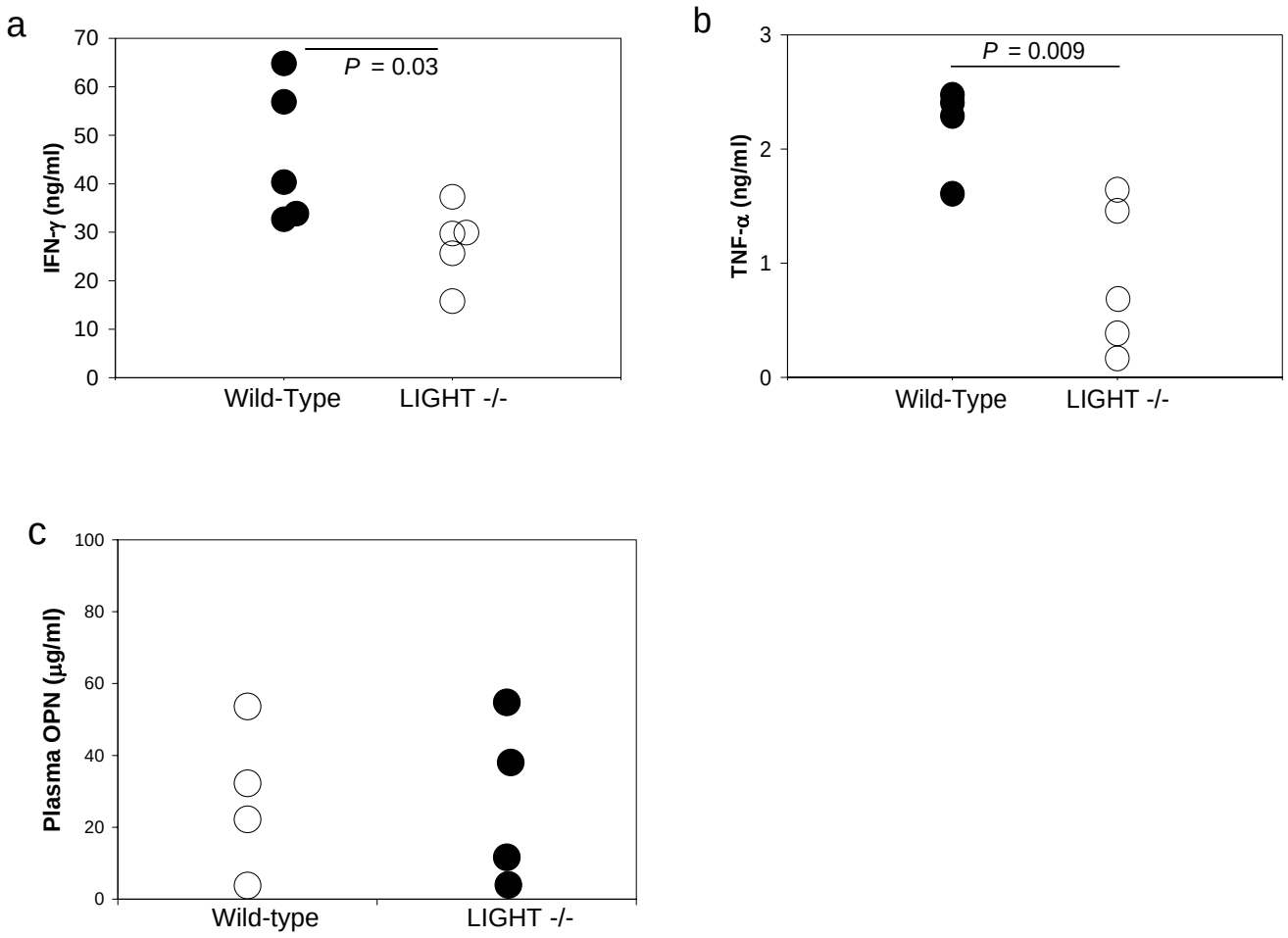
Supplementary Figure 5. Dispensable role of NKT cells in the cleavage of LIGHT

B6 mice were injected i.p with 500 μg of either control antibody or anti-NK1.1 antibody (PK136) on days 0 and 3. On day 4, the mice were injected with a sublethal dose of ConA (12.5 mg/kg) along with 20 μg of LIGHT plasmid by hydrodynamic injection. Soluble LIGHT levels were measured 18 hours post injection.



Supplementary Figure 6. Potential of LIGHT to mediate hepatitis independently of ConA or the presence of lymphocytes

(a) B6 mice were injected with either 20 μg of LIGHT plasmid or empty vector by hydrodynamic injection. Sera were collected 18 hours post injection and ALT was measured as described in the materials and methods. Pooled data from 3 independent experiments is shown. (b) *Rag*$^{-/-}$ mice were injected with 20 μg of control vector or LIGHT-encoding plasmid by hydrodynamic injection in combination with sublethal dose of ConA (12.5 mg/kg). Mouse sera were collected 18 hours later and ALT levels were measured.



Supplementary Figure 7. Decreased production of IFN-γ and TNF-α in LIGHT-deficient mice
Wild-type or LIGHT-deficient B6 mice were injected with a lethal dose of ConA (25mg/kg) and their cytokine levels were monitored at different time points. (a) IFN-γ was measured from sera at 8 hours using a kit from BD Biosciences. (b) TNF-α was measured from sera at 2 hours using a kit from e-bioscience. (c) Osteopontin (OPN) was measured from plasma at 24 hours post injection using a kit from IBL Co. Ltd.