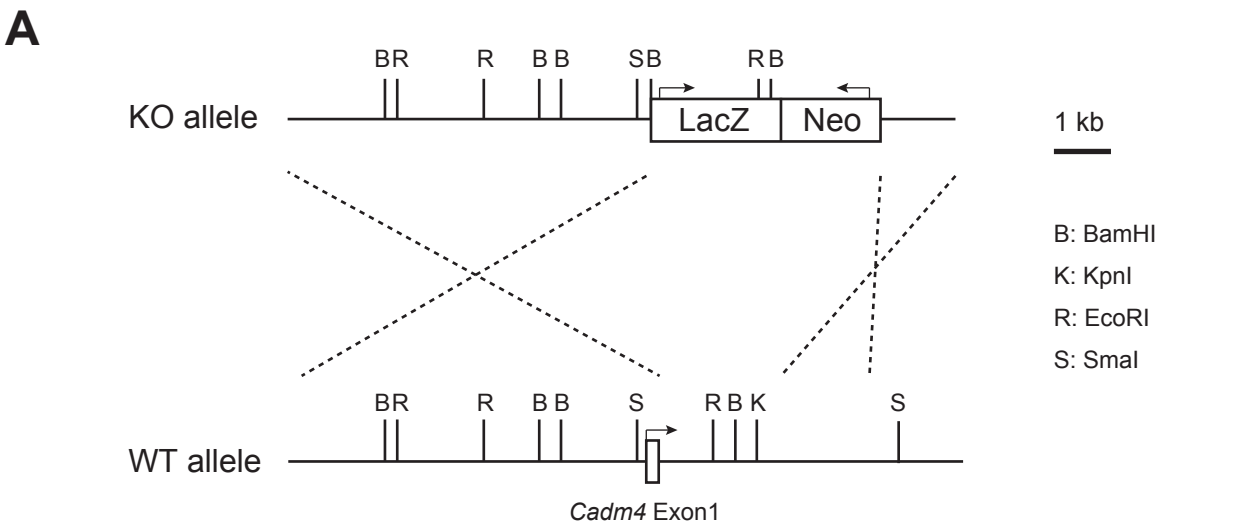
Figure S1



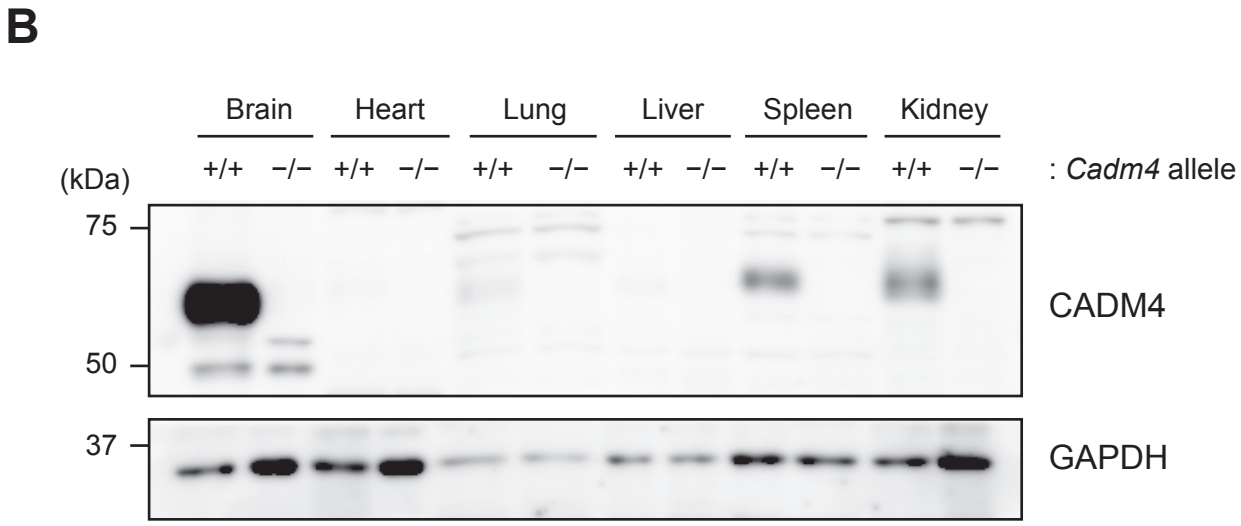


Figure S1. Generation of a *Cadm4*-knockout mouse. (**A**) Targeting construct of the mouse *Cadm4* gene. A white box represents exon 1 and restriction enzyme sites are indicated. The LacZ-Neo cassette replaces the coding region of exon 1 and part of intron 1 of the *Cadm4* gene. (**B**) Western blotting of CADM4 in various organs from a wild-type and a *Cadm4*-knockout mice. Strong expression of CADM4 was observed in the brain, mild expression was observed in the spleen and kidney, and weak expression was observed in the lung and liver in a wild-type mouse. The expression of CADM4 was not detected at all in a *Cadm4*-knockout mouse.

Figure S2

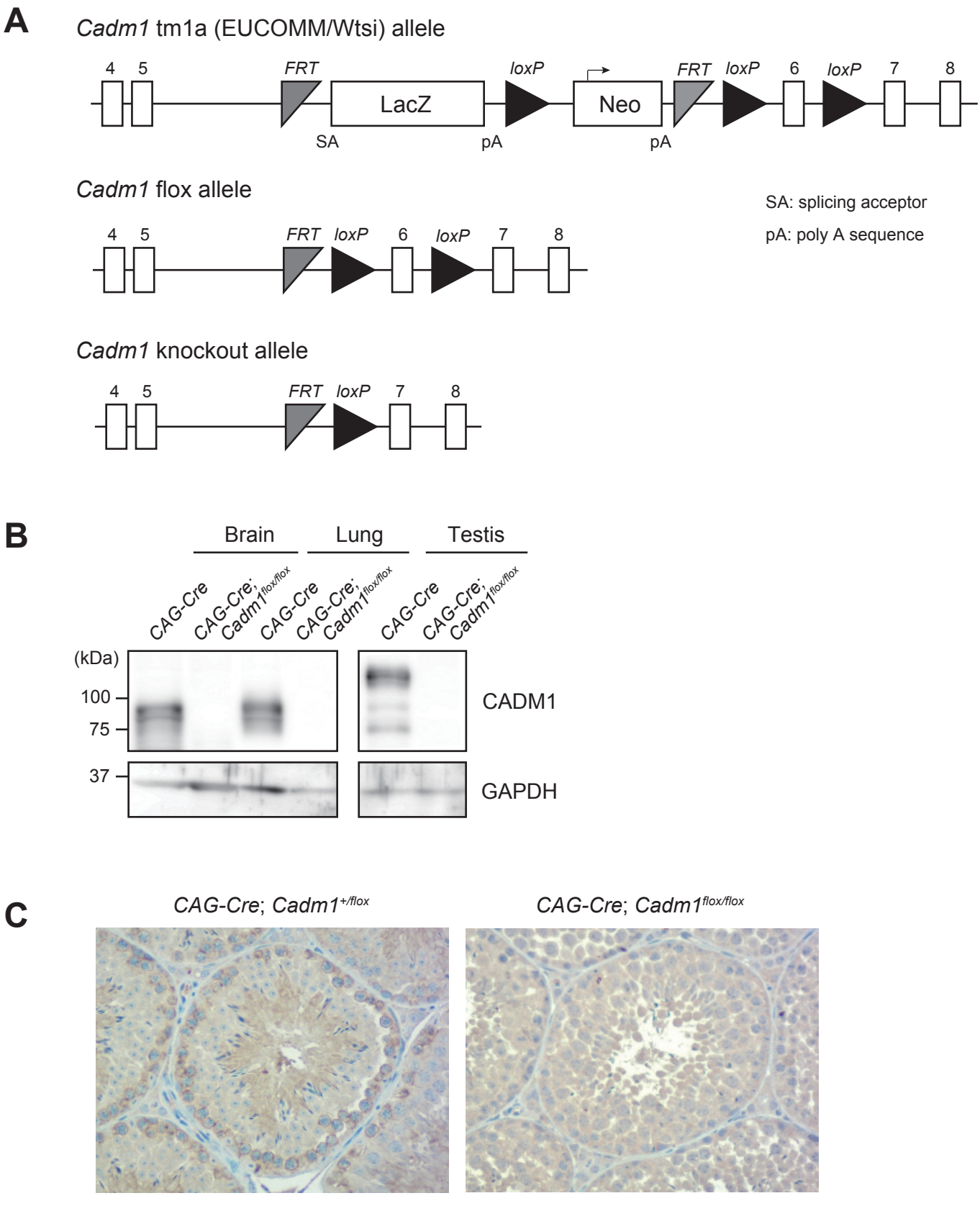


Figure S2. Generation of a *Cadm1* conditional knockout mouse. (**A**) Schematic diagrams of the conditional and knockout alleles of the *Cadm1* gene. *Cadm1*$^{+/tm1a(EUCOMM/Wtsi)}$ mice were crossed with *CAG-FLP* mice to generate *Cadm1*$^{+/flox}$ mice. Deletion of *Cadm1* exon 6 mediated by Cre recombinase results in a frameshift. (**B**) Western blotting of CADM1 in the brain, lung, and testis from a *CAG-Cre* and a *CAG-Cre*; *Cadm1*$^{flox/flox}$ mice. The expression of CADM1 was not detected at all in a *CAG-Cre*; *Cadm1*$^{flox/flox}$ mouse. (**C**) Immunohistochemistry of CADM1 in the mouse testes. The expression of CADM1 was observed in spermatogonia and spermatids in the testis of a *CAG-Cre*; *Cadm1*$^{+/flox}$ mouse (left), while the signal of CADM1 was not detected in the testis and mature spermatids were rarely observed in the seminiferous tubules of a *CAG-Cre*; *Cadm1*$^{flox/flox}$ mouse (right).

Figure S3

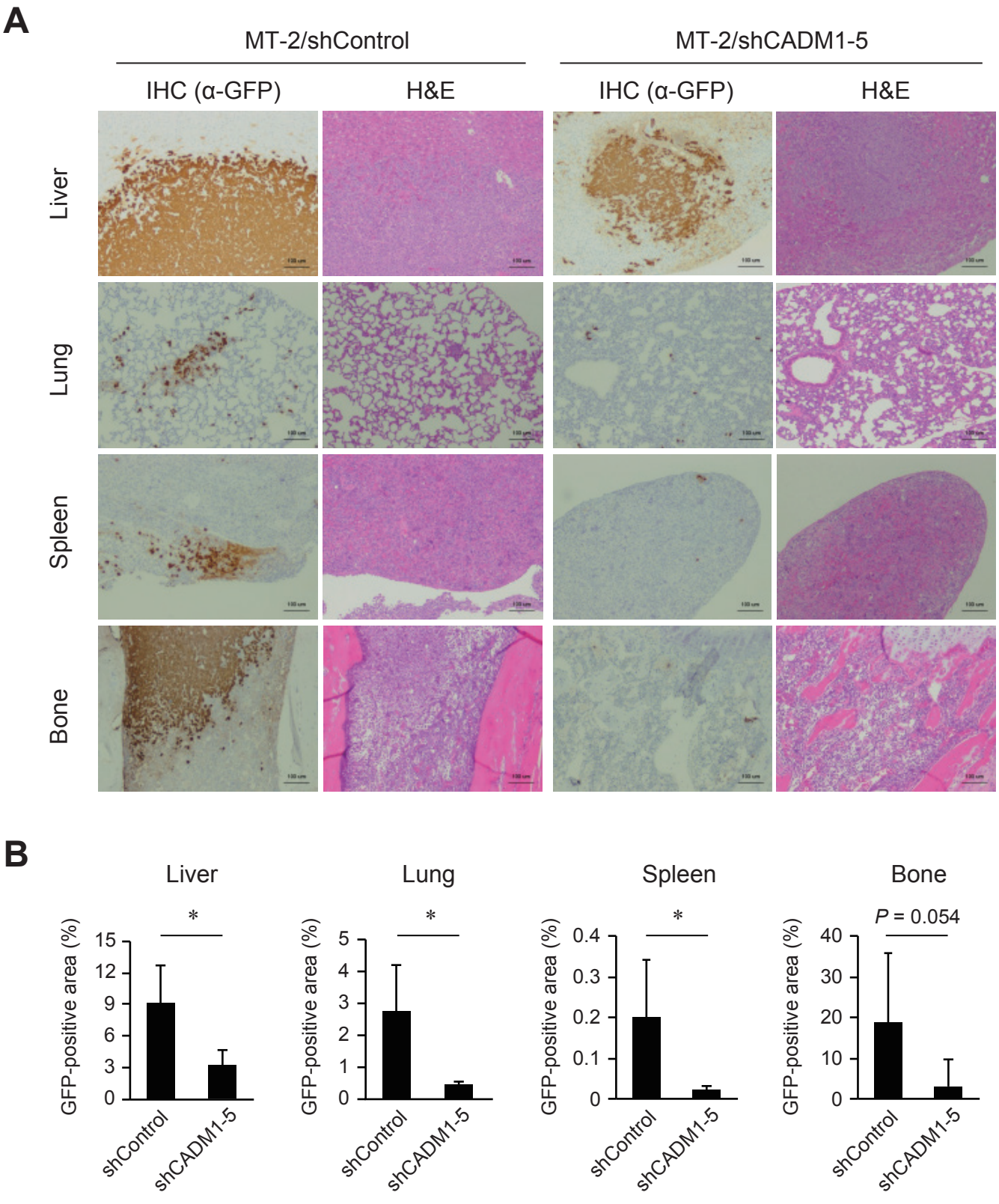


Figure S3. Knockdown of CADM1 in HTLV-I–transformed T cells attenuated infiltration into multiple organs. (**A**) Histological examination of MT-2/shControl and MT-2/shCADM1-5 cells infiltrated into the liver, lung, spleen, and bone of NOG mice. H&E staining and immunohistochemistry using an anti-GFP antibody for detecting MT-2 cells were shown. Magnification, ×100; Bars, 100 μm. (**B**) The infiltration of MT-2 cells into the liver, lung, spleen, and bone was quantified as the percentage of GFP-positive tissue area. Means ± SD for each organ from five mice were shown. *, $P < 0.05$ by *t*-test.

Figure S4

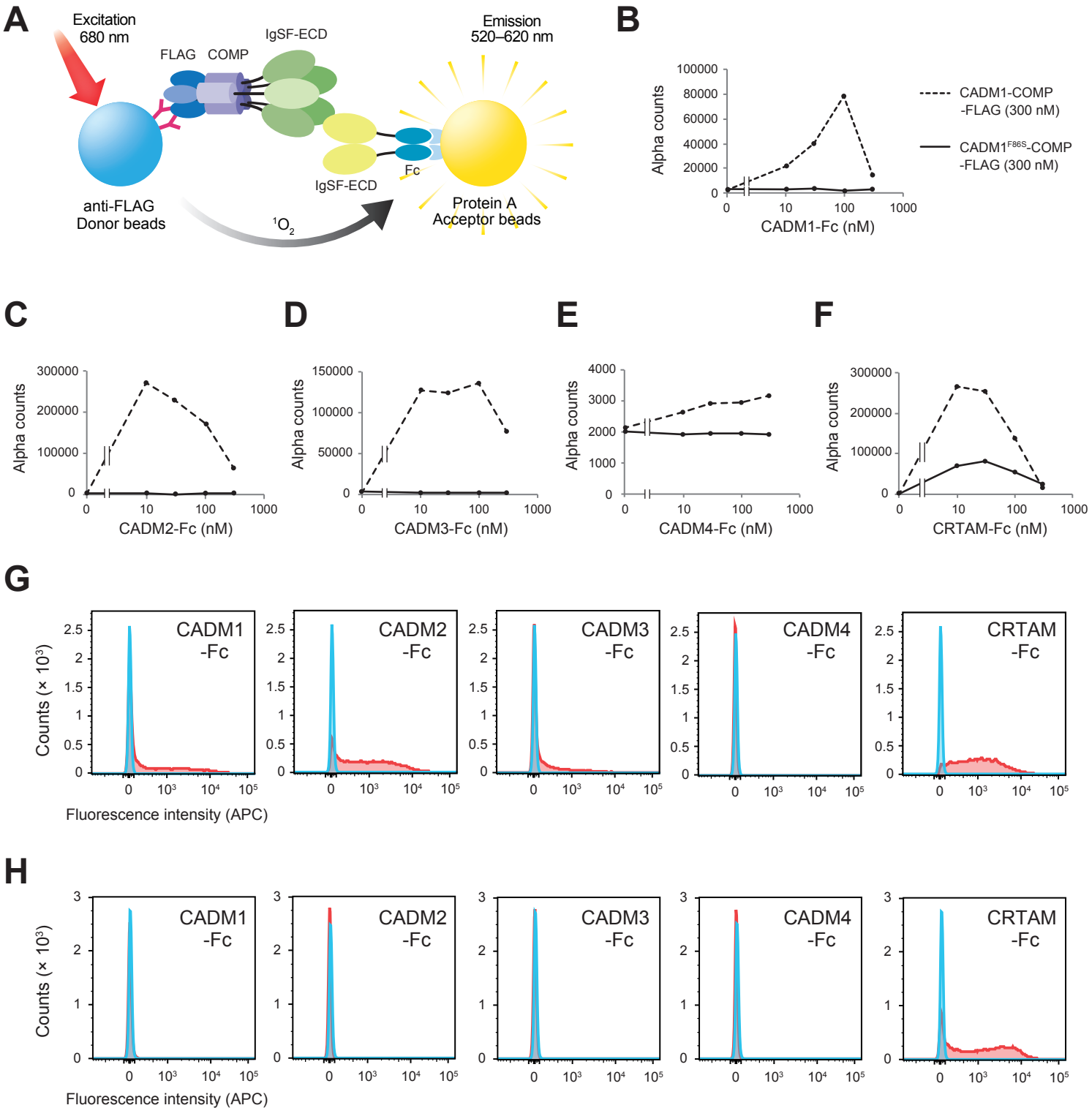


Figure S4. Interaction analyses of CADM1^{F86S} mutant with known CADM1-binding proteins. (**A**) Schematic diagram of the detection system of extracellular protein–protein interactions using Alpha technology. A tag consisting of pentamarization domain of rat cartilage oligomeric matrix protein (COMP) followed by FLAG was fused to the extracellular domain (ECD) of one protein, whereas human IgG_2-Fc tag was fused to the ECD of the other protein. The interaction of these two proteins was detected by a luminescence signal created by a cascade of chemical reactions between Protein A donor beads and anti-FLAG acceptor beads. (**B–F**) Interaction analyses of CADM1 mutant with known CADM1-binding proteins using Alpha technology. The binding of CADM1 or CADM1^{F86S} fused to COMP-FLAG tag with increasing amounts of CADM1-Fc (**B**), CADM2-Fc (**C**), CADM3-Fc (**D**), CADM4-Fc (**E**), and CRTAM-Fc (**F**) was examind. (**G, H**) Binding analysis of CADM1 (**G**) and CADM1^{F86S} (**H**) with known CADM1-binding proteins on the cell surface. EL4/CADM1 or CADM1^{F86S} cells were incubated with the indicated proteins and an APC-onjucated anti-Fc antibody, and then the binding of the proteins was detected by flow cytometry. Histograms of cell counts treated with IgG (blue) or the indicated proteins (red) were shown.

Figure S5

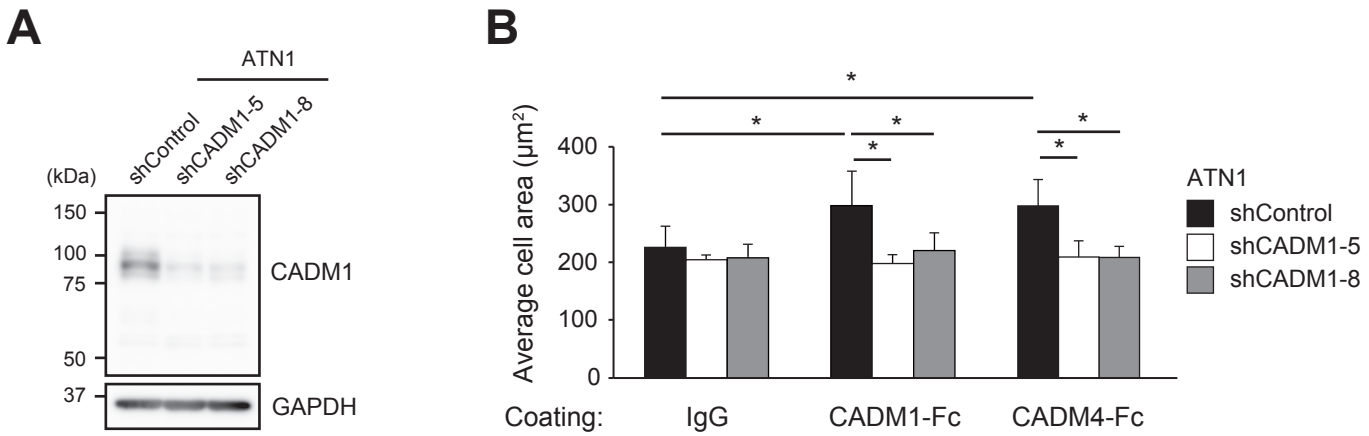
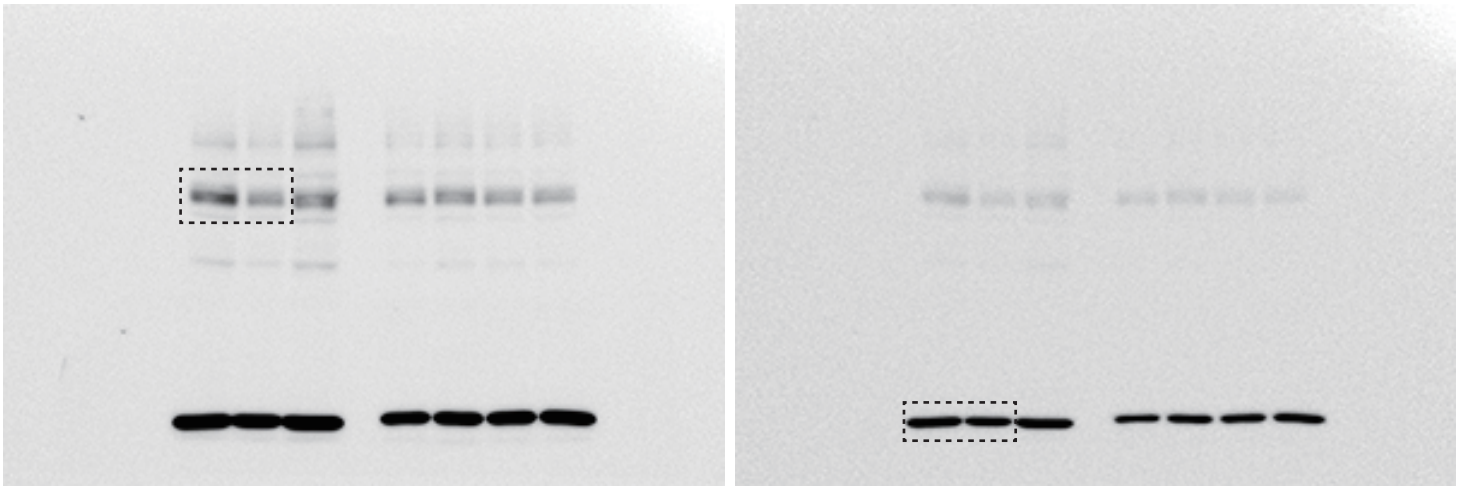


Figure S5. Knockdown of CADM1 attenuated cell extension of ATL cells. (**A**) CADM1 was stably knocked down in ATN1 cells by two individual shRNA. (**B**) Spreading of ATN1 cells when incubated on IgG, CADM1-Fc, or CADM4-Fc. ATN1 cells were incubated on coverslips coated with the indicated proteins, and cell spreading was quantified by measuring the area of 100 cells in an assay. Means ± SD of average cell area in three independent experiments was shown. *, $P < 0.05$ by *t*-test.

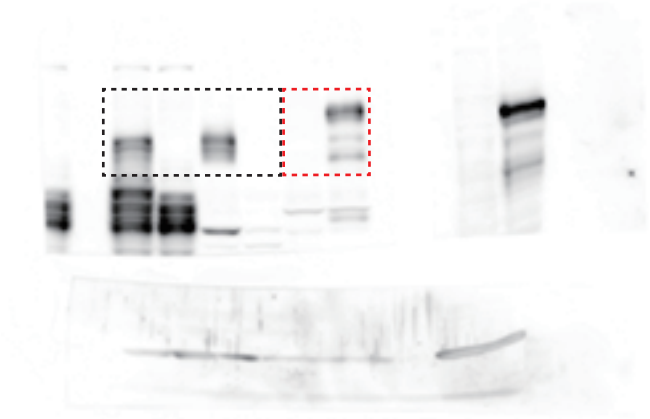
Figure S6

A

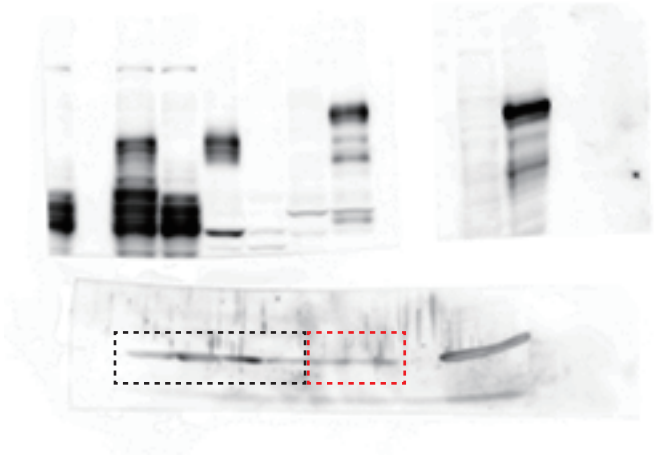


CADM1 GAPDH

B



CADM1



GAPDH

C

CADM1 (upper), GAPDH (lower)

Figure S6. Raw images of Western blotting. Dotted boxes indicate the cropped images used in Figure 1E (**A**), Figure S2B (**B**), and Figure S5A (**C**). The images in red dotted boxes in panel (B) were shown as mirror images in Figure S2B.