

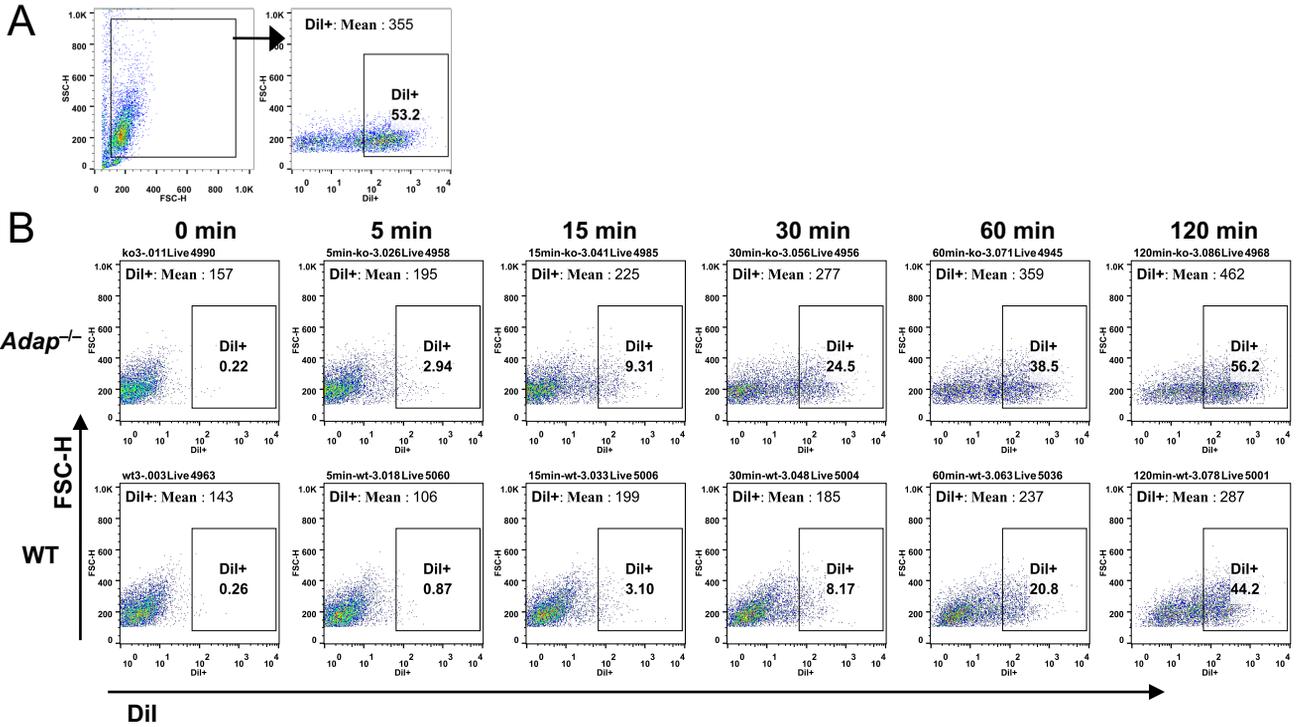
Supplemental Figure 1. ADAP underexpression is associated with thrombocytopenia.

A ADAP expression in different tissues of WT and *Adap*^{-/-} mice (KO).

B WT and *Adap*^{-/-} mice were treated with saline, or a daily low-dose of anti-GPIIb antibody MWRReg30 (anti-CD41, IgG1) via i.v. as indicated (n = 4 mice in each group). Platelet counts were enumerated over a time course of 3 days and presented as percentages of those prior to antibody injection at Day 0.

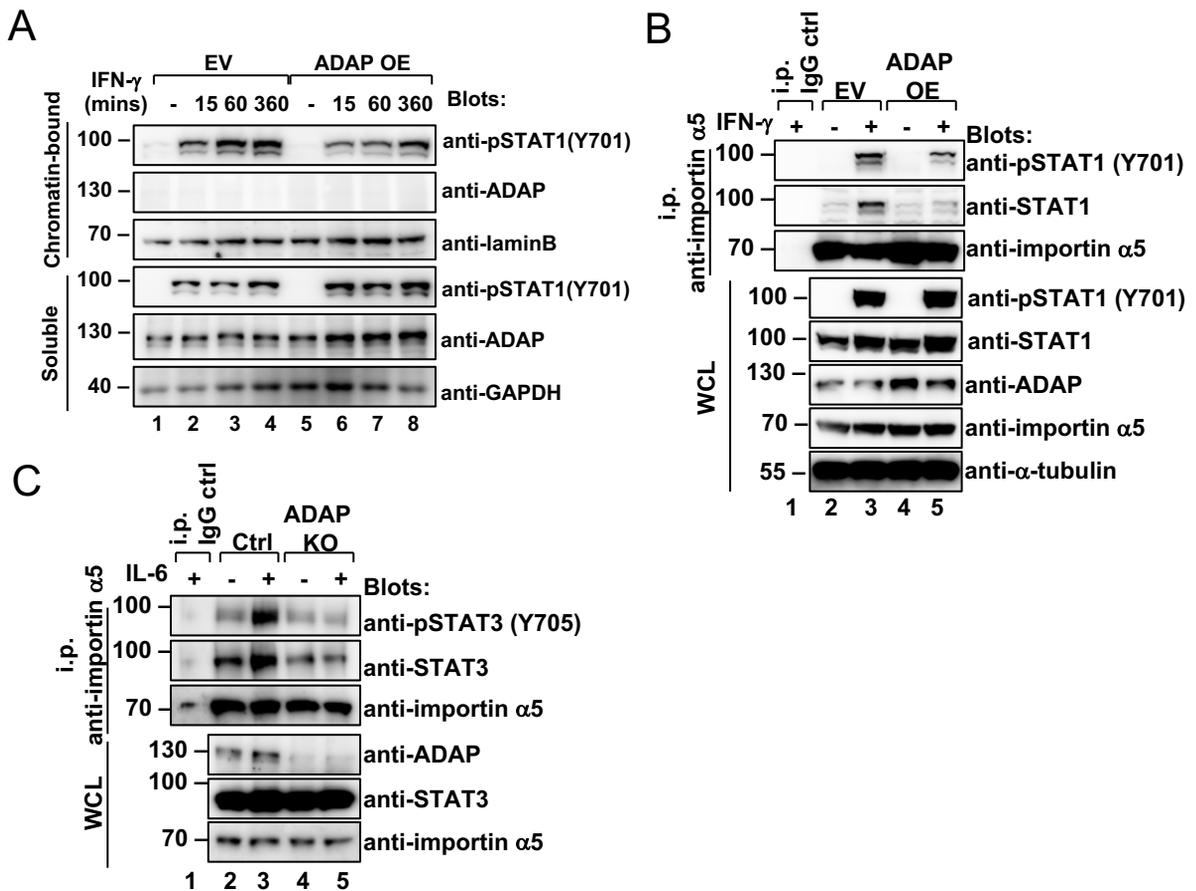
C Flow cytometric analysis of antiplatelet antibody in the sera of WT and *Adap*^{-/-} mice. Washed platelets were incubated with sera from WT mice (n = 10) and *Adap*^{-/-} mice (n = 10), or BSA as a negative control, and stained with Alexa Fluor 647 anti-mouse IgG. The percentages of Alexa Fluor 647-positive platelet were plotted on the right panel.

D Flow cytometric analysis of tissue-resident macrophage (CD11b^{hi}F4/80^{hi}) in the spleen, liver, lung, and kidney, or monocyte-derived macrophage (CD11b^{hi}F4/80^{int}) in the bone marrow from mice intravenously injected with either clodronate liposomes or PBS liposomes as a control (n = 4, Mann-Whitney U test). The macrophage frequencies in the spleen, liver, and bone marrow were largely decreased at two days after clodronate liposome injection.



Supplementary Figure 2. Gating strategy and representative plots for the *in vitro* phagocytosis assay by flow cytometry.

A-B Gating strategy (A) and representative plots (B) for the *in vitro* phagocytosis assay as shown in Figure 2A. The percentage and the mean fluorescence intensity of Dil-positive cells were determined. The phagocytic index was calculated as the mean fluorescence intensity multiplied by the percentage of Dil-positive cells.

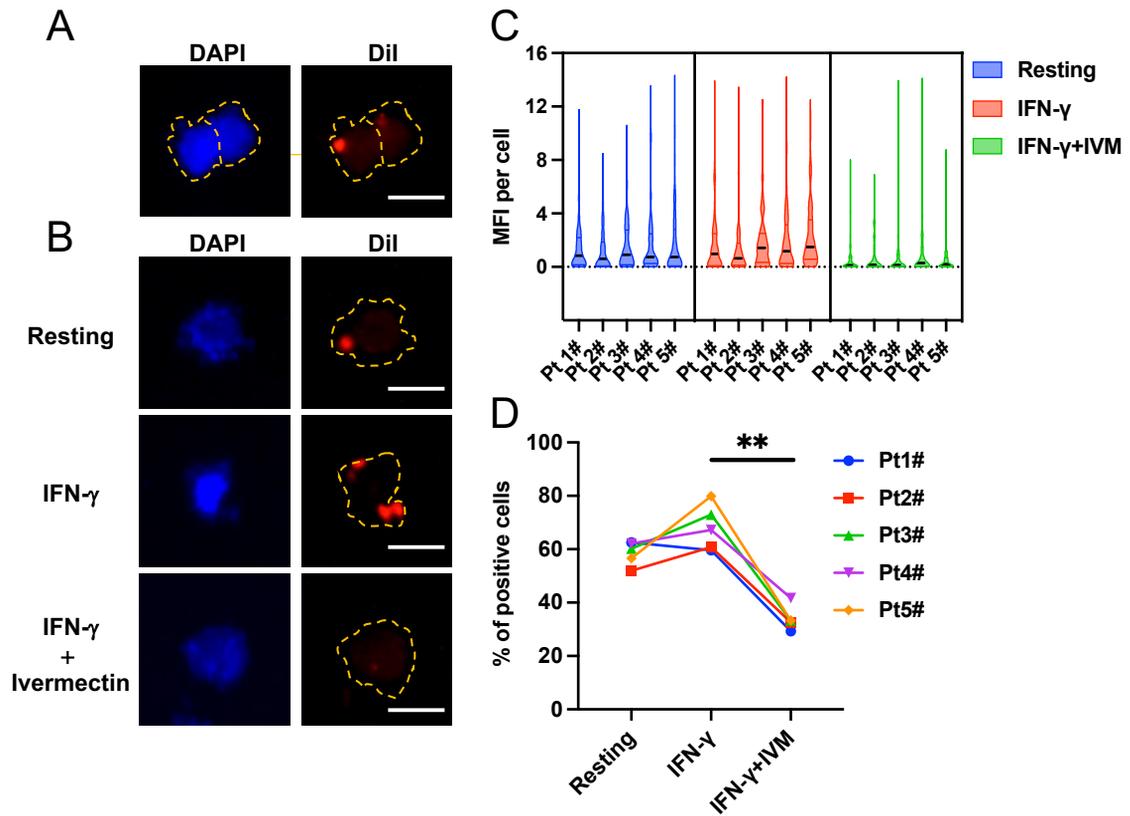


Supplementary Figure 3. ADAP negatively targets STAT1/impartin α 5 module but not STAT3 /impartin α 5.

A Immunoblot analysis of pY701-STAT1 in soluble and chromatin-bound fractions in empty vector- or ADAP-overexpressed (OE) RAW264.7 cells. Cells were stimulated with IFN- γ at the indicated time points and subjected to cellular fractionation, followed by Western-blot analysis with indicated antibodies.

B Immunoprecipitation and immunoblot analysis of the STAT1/ impartin α 5 interaction in empty vector- or ADAP-overexpressed RAW264.7 cells with or without IFN- γ stimulation.

C The effects of ADAP deficiency on the interaction between STAT3 and impartin α 5 in response to IL-6 stimulation. The interaction between STAT1 and impartin α 5 was determined by immunoprecipitation with anti-impartin α 5, followed by immunoblotting with pY701-STAT1 antibody in WT or ADAP-KO RAW264.7 cells.



Supplemental Figure 4. *In vitro* phagocytosis of Dil-labelled anti-SRBC IgG-opsonized SRBCs by monocyte-derived macrophages from ITP patients.

A-D In relation to Figure 6F, monocyte-derived macrophages from 5 ITP patients were subjected to stimulation as indicated before incubation with Dil-labelled and anti-SRBC opsonized SRBC for 2 hr. Nuclei were stained with DAPI and cells were outlined by dashed lines (**A-B**), within which the MFI of each cell is determined and plotted in the violin plot (**C**). A total of approx. 100 cells in each group were analysed. The percentages of SRBC-phagocytosed monocyte-derived macrophages in each group were plotted in the histogram in **D** ($n = 5$, one-way ANOVA, Tukey's multiple comparison). Scale bars denote 5 μm .

Supplemental Table 1. Demographic and clinical characteristics of patients with ITP and splenic trauma.

Patient ID	Age	Sex	platelet count (10 ⁹ /L)		Prior treatment	Disease duration (year)
			pre-splenectomy	1 week post-splenectomy		
1	25	F	14	165	steroids	1+
2	31	M	50	139	steroids, IVIg	2+
3	13	M	75	838 ^a	steroids, herbs, CsA	5+
4	45	M	40	258	steroids, herbs,	1+
5	73	M	35	20 ^a	steroids	1+
6	40	M	9	396	steroids	1+
7	71	M	90	90	steroids, herbs, IVIg	1+
8	62	F	10	372 ^a	steroids, IVIg	7+
9	28	M	74	109	steroids	1+
10	34	F	19	112 ^a	steroids	4+
11	19	F	128	430	/	/
12	47	M	235	110	/	/
13	56	M	101	101	/	/
14	57	M	111	135	/	/
15	58	M	159	127	/	/
16	61	F	139	115	/	/
17	34	F	246	173	/	/
18	48	M	409	200	/	/
19	55	M	187	158	/	/
20	53	M	248	229	/	/
21	17	M	395	265	/	/
22	51	F	289	334	/	/
23	72	M	121	166	/	/
24	38	M	253	333	/	/
25	46	M	207	375	/	/
26	25	M		29	steroids, TPO, IVIg	1-
27	71	M		8	steroids, TPO, IVIg	1-
28	20	F		95	steroids, IVIg, CD20	1-
29	38	F		85	steroids, TPO, IVIg	1-
30	56	F		3	steroids, TPO, CsA, Herombopag	5+

^a within two weeks post-splenectomy

IVIg, intravenous immunoglobulin; CsA, Cyclosporin A; TPO, thrombopoietin

Steroids include dexamethasone, prednisone, danazol, hydrocortisone

Patient ID 1-10: ITP patients with splenectomy; 11-25: non-ITP patients with splenic trauma; 26-30: ITP patients providing PBMC

Supplemental Table 2. Antibodies list.

Antibodies	CLONE	SOURCE	IDENTIFIER
Rabbit anti-Stat1 antibody	n/a	Cell Signaling Technology	Cat# 9172, RRID: AB_2198300
Rabbit anti-Phospho-Stat1 (Tyr701) Antibody	58D6	Cell Signaling Technology	Cat# 9167, RRID:AB_561284
Rabbit anti-Phospho-Stat1 (Ser727) Antibody	n/a	Cell Signaling Technology	Cat# 9177, RRID:AB_2197983
Rabbit anti-GAPDH Antibody	D16H11	Cell Signaling Technology	Cat# 5174, RRID:AB_10622025
Rabbit anti-Phospho-p44/42 MAPK (Erk1/2) (Thr202/Tyr204) antibody	D13.14.4E	Cell Signaling Technology	Cat# 4370, RRID:AB_2315112
Rabbit anti-p44/42 MAPK (Erk1/2) antibody	137F5	Cell Signaling Technology	Cat# 4695, RRID:AB_390779
Rabbit anti-Phospho-p38 MAPK (Thr180/Tyr182) antibody	D3F9	Cell Signaling Technology	Cat# 4511, RRID:AB_2139682
Rabbit anti-p38 MAPK antibody	D13E1	Cell Signaling Technology	Cat# 8690, RRID:AB_10999090
Rabbit anti-Akt (pan) antibody	C67E7	Cell Signaling Technology	Cat# 4691, RRID:AB_915783
Rabbit anti-Integrin β 3 antibody	D7X3P	Cell Signaling Technology	Cat# 13166, RRID:AB_2798136
Rabbit anti-Phospho-Stat-3 (tyr705) antibody	n/a	Cell Signaling Technology	Cat# 9131, RRID:AB_331586
Rabbit anti-Stat3 Antibody	n/a	Cell Signaling Technology	Cat# 9132, RRID:AB_331588
Anti-rabbit IgG (H+L), F(ab) 2 Fragment (Alexa Fluor 555 Conjugate) antibody	n/a	Cell Signaling Technology	Cat# 4413, RRID:AB_10694110
Anti-mouse IgG, HRP-linked Antibody	n/a	Cell Signaling Technology	Cat# 7076, RRID:AB_330924
Anti-rabbit IgG, HRP-linked Antibody	n/a	Cell Signaling Technology	Cat# 7074, RRID:AB_2099233
Rabbit anti-ADAP / SLAP-130 / Fyb antibody	n/a	Millipore	Cat# 07-546, RRID:AB_310704
Mouse anti-HA antibody	HA-7	Sigma-Aldrich	Cat# H9658, RRID:AB_260092
Mouse anti-FLAG antibody	M2	Sigma-Aldrich	Cat# F1804, RRID:AB_262044
Rabbit anti-alpha Tubulin antibody	n/a	Abcam	Cat# ab4074, RRID:AB_2288001
Alexa Fluor 488-conjugated anti-CD68	KP1	Abcam	Cat# ab222914
Rabbit anti-Phospho-SHP-1 (Tyr536) Antibody	n/a	Absin	Cat# abs130871
Mouse anti-p-Akt1/2/3 Antibody	B-12	Santa Cruz Biotechnology	Cat# sc-377556
IRDye 800CW Donkey anti-Rabbit IgG antibody	n/a	LI-COR	Cat# 926-32213, RRID:AB_621848
IRDye 680RD Goat anti-Mouse IgG antibody	n/a	LI-COR	Cat# 926-68070, RRID:AB_10956588
Rabbit anti-Importin Alpha 5 antibody	n/a	Proteintech	Cat# 18137-1-AP, RRID:AB_2133553
Alexa Fluor 647-conjugated anti-F4/80 antibody	T45-2342	BD Bioscience	Cat# 565853, RRID:AB_2744474
PE-conjugated Anti-Mouse CD64.1/Fc γ RI	X54-5/7.1.1	BD Bioscience	Cat# 558455, RRID:AB_647241
FITC-conjugated anti-CD41	MWReg30	BD Bioscience	Cat# 553848, RRID:AB_395085
FITC-conjugated anti-mouse CD11b	M1/70	BD Bioscience	Cat# 557396, RRID:AB_396679
PE-conjugated anti-mouse CD45	30-F11	BD Bioscience	Cat# 553081, RRID:AB_394611
FITC-conjugated anti-mouse CD3	17A2	BD Bioscience	Cat# 555274, RRID:AB_395698
PerCP-Cy5.5-conjugated anti-mouse CD4	RM4-5	BD Bioscience	Cat# 561115, RRID:AB_10563934
APC-conjugated anti-mouse CD8a	53-6.7	BD Bioscience	Cat# 553035, RRID:AB_398527
Ultra-LEAF Purified anti-mouse CD4 antibody	GK1.5	BioLegend	Cat# 100442, RRID:AB_11149488
Ultra-LEAF Purified anti-mouse CD8a antibody	53-6.7	BioLegend	Cat# 100746, RRID:AB_11147171
purified anti-mouse CD20	SA271G2	BioLegend	Cat# 152102, RRID:AB_2632610
Ultra-LEAF Purified Rat IgG2b, kappa Isotype Ctrl antibody	n/a	BioLegend	Cat# 400644, RRID:AB_11149687
Purified anti-mouse CD32 (Fc γ r2) antibody	S17012B	BioLegend	Cat# 156402, RRID:AB_2783133
PE anti-mouse CD16.2 (Fc γ maRIV) antibody	9E9	BioLegend	Cat# 149504, RRID:AB_2565811
PE anti-rat IgG2b antibody	MRG2b-85	BioLegend	Cat# 408214, RRID:AB_2749893
FITC anti-mouse MERTK (Mer) antibody	2B10C42	BioLegend	Cat# 151503, RRID:AB_2617034
PE anti-mouse CD19 antibody	1D3/CD19	BioLegend	Cat# 152407, RRID:AB_2629816
Ultra-LEAF Purified anti-mouse CD41 antibody	MWReg30	BioLegend	Cat# 133940, RRID:AB_2810396
Antibodies for Platelet Depletion in Mice antibody	n/a	Emfret	Cat# R300, RRID:AB_2721041
PE anti-CD16/FCGR3 antibody	#002	Sino Biological	Cat# 50326-R002-P
FITC-conjugated streptavidin	n/a	eBioscience	Cat# 11-4317-87
Goat Anti-Mouse IgG (H+L) Antibody, Alexa Fluor-647 Conjugated	n/a	Molecular Probes	Cat# A-21235, RRID:AB_2535804