Supplementary Table 1. Antibodies and conditions for western blot analysis.

Antibody	Animal	Company	Clone or Catalog #	Dilution	Reaction
Cyclin D1	Rabbit mAb	Abclonal Technology	A10038	x 1,000	RT, 60 mins
Cyclin A2	Rabbit mAb	Abclonal Technology	A19036	x 1,000	RT, 60 mins
Cyclin B1	Rabbit mAb	Abclonal Technology	A19037	x 1,000	RT, 60 mins
CDK1	Rabbit mAb	Abclonal Technology	A11420	x 1,000	RT, 60 mins
CDK2	Rabbit Poly	Abclonal Technology	A18000	x 1,000	RT, 60 mins
CDK4	Rabbit Poly	Abclonal Technology	A0366	x 1,000	RT, 60 mins
β-actin	Rabbit Poly	Abclonal Technology	AC006	x 1,000	RT, 60 mins

Supplementary Table 2. Antibodies and conditions for immunohistochemical analysis.

Antibody	Animal	Company	Clone or Catalog #	Unmasking	Dilution	Reaction
MPO	Rabbit Poly	Thermo Scientific	Ab-1	CB (pH 6.0)	x 50	RT, 60 mins
iNOS	Rabbit Poly	Abcam	ab15323	CB (pH 6.0)	x 50	RT, 60 mins
Arginase-1	Rabbit mAb	Cell Signaling Technology	D4E3M; #93668	CB (pH 6.0)	x 400	RT, 60 mins
CD8	Rabbit Poly	Abcam	ab203035	CB (pH 6.0)	x 500	RT, 60 mins
CD45R	Rat mAb	BD Pharmingen	B220	ProK	x 200	RT, 60 mins
K-19	Rat mAb	DSHB	TOROMA III; AB_2133570	CB (pH 6.0)	x 200	RT, 60 mins
Ki-67	Rabbit Poly	Abcam	ab66155	CB (pH 6.0)	x 100	RT, 60 mins
Cyclin D1	Rabbit mAb	Abclonal Technology	A10038	CB (pH 6.0)	x 200	RT, 60 mins
Cyclin A2	Rabbit mAb	Abclonal Technology	A19036	CB (pH 6.0)	x 200	RT, 60 mins
Cyclin B1	Rabbit Poly	Santa Cruz Biotechnology, Inc	sc-752	CB (pH 6.0)	x 100	RT, 60 mins
CD31	Rabbit Poly	Abcam	ab28364	TE (pH 9.0)	x 100	RT, 60 mins
αSMA	Pabbit Poly	Abcam	ab5694	CB (pH 6.0)	x 50	4°C , O/N

* ProK, pretreated with proteinase K (Ready-to-Use, Dako, Japan, Tokyo) for 10 mins at RT; CB, incubate at 105°C for 10 mins in 0.01 M Citrate buffer (pH 6.0); TE, incubate at 120 °C for 10 mins in Tris-EDTA buffer (pH 9.0; Nichirei Bioscience Inc. Tokyo, Japan)

Supplementary Table 3. Phenotype of *KPPC and normal control* mice with/without administration of mirogabalin.

No.	ID #	Age (days)	Sex	Body weight (g) *	Mouse	Administration	Histological phenotype **	Pancreatic weight (mg)	Tumour size (mm) and Location ***	Direct invasion	Metastasis/Dissemination
1	303	55	M	ND	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	1644.8	10 x 10 x 12 (H/B)	Pancreatic LN	Liver, spleen, adipose tissue around kidney, diaphragm, para-oesophagus, LNs, Peripheral nerves, ganglia
2	305	48	M	ND	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	526.2	7 x 7 x 5 (H)	Duodenum	Liver, dissemination (mesenterium, kidney, diaphragm), LNs
3	354	57	M	17.8	*KPPC*	Vehicle	PDAC, poorly + focal anaplastic carcinoma	985.5	10 x 6 x 5 (H)	Duodenum	No
4	369	64	M	14.5	*KPPC*	Vehicle	PDAC, poorly/sarcomatoid + focal anaplastic carcinoma	802.5	3 x 5 x 2 (H); 6 x 5 x 3 (B); 4 x 5 x 3 (T)	Duodenum, bile duct	No
5	373	53	F	19.7	*KPPC*	Vehicle	PDAC, moderately to poorly/sarcomatoid + focal anaplastic carcinoma	1273.3	11 x 10 x 9 (B/T)	No	No
6	383	70	F	ND	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	2200.1	15 x 12 x 7 (H/B); 14 x 12 x 7 (T)	No	Dissemination (liver, spleen, kidneys, adrenal gland), LNs, lung, muscle, submandibular gland
7	403	58	M	24.4	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	1373.8	3 x 5 x 4 (H); 7 x 8 x 5 (H); 8 x 10 x 10 (B)	No	No
8	406	69	M	23.3	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	1651.2	11 x 8 x 8 (H/B); 7 x 8 x 5 (B); 7 x 7 x 8 (T)	Duodenum	No
9	408	64	F	12.3	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	1205.6	6 x 7 x 6 (H); 7 x 8 x 7 (H)	Duodenum, bile duct	Dissemination (mesenterium), LNs
10	466	55	M	ND	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	1322.8	10 x 8 x 7 (H/B)	Pancreatic LN	Lung, adipose tissue around kidney, LNs
11	996	65	M	25.6	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	1557.5	8 x 8 x 7 (H), 6 x 5 x 5 (H), 12 x 5 x 5 (T)	Common dile duct, gastric wall	No
12	997	69	M	26.5	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	1569.6	6 x 5 x 5 (H), 8 x 6 x 6 (H), 8 x 5 x 5 (H), 4 x 4 x 4 (T)	Peripheral nerves	LN (mesenteric, gastric)
13	1001	69	F	19.1	*KPPC*	Vehicle	PDAC, moderately to poorly + focal anaplastic carcinoma	1127.9	10 x 9 x 8 (H), 6 x 6 x 5 (T)	Duodenum	No
14	1026	60	M	17.8	*KPPC*	Vehicle	PDAC, moderately to poorly + anaplastic carcinoma	2265.6	12 x 10 x 10 (H)	Duodenum	LN (mesenteric)
1	1072	68	M	23.1	*KPPC*	Mirogabalin	PDAC, moderately to poorly/sarcomatoid + focal anaplastic carcinoma	2270.1	23 x 8 x 7 (B/T), 10 x 10 x 7 (H)	Pancreatic LN	No
2	1073	66	F	20.6	*KPPC*	Mirogabalin	PDAC, moderately to poorly/sarcomatoid + focal anaplastic carcinoma	3745.0	14 x 16 x 10 (T), 5 x 5 x 5 (H)	Pancreatic LN	Lung, liver, dissemination (stomach, kidney)
3	1080	72	F	19.1	*KPPC*	Mirogabalin	PDAC, moderate to poorly/sarcomatoid + focal anaplastic carcinoma	1652.1	12 x 10 x 9 (B), 8 x 6 x 5 (H), 11 x 10 x 5 (H)	Pancreatic LN	No
4	1098	58	M	21.4	*KPPC*	Mirogabalin	PDAC, moderately to poorly/sarcomatoid + focal anaplastic carcinoma	1697.9	14 x 12 x 6 (H/B), 6 x 6 x 5 (H)	Duodenum	Lung, hepatic hilar LNs
5	1106	74	M	21.9	*KPPC*	Mirogabalin	PDAC, moderately to poorly/sarcomatoid + focal anaplastic carcinoma	4775.5	12 x 11 x 8 (T), 15 x 13 x 10 (H/B)	Duodenum, spleen	Dissemination (adrenal glands, diaphragm, liver, stomach, epididymis, adipose tissue around kidney, iliopsoas)
6	1128	66	M	22.3	*KPPC*	Mirogabalin	PDAC, moderately to poorly/sarcomatoid + focal anaplastic carcinoma	1295.6	10 x 10 x 5 (B), 3 x 3 x 3 (T)	No	Dissemination (mesenterium), LNs (mesenteric, hepatic hilar)
7	1147	71	M	26.4	*KPPC*	Mirogabalin	PDAC, moderate to poorly/sarcomatoid + focal anaplastic carcinoma	1382.8	18 x 10 x 7 (B/H), 4 x 5 x 3 (H)	No	No
8	1149	67	M	22.1	*KPPC*	Mirogabalin	PDAC, moderately to poorly/sarcomatoid + focal anaplastic carcinoma	1852.9	10 x 10 x 7 (H/B), 8 x 6 x 6 (H)	Duodenum, pancreatic LN	Dissemination (adipose tissue around kidney, Diaphragm), LNs (mesenteric, gastric, hepatic hilar)
9	1163	64	F	21.8	*KPPC*	Mirogabalin	PDAC, moderately to poorly/sarcomatoid + focal anaplastic carcinoma	1139.9	5 x 5 x 5 (H), 11 x10 x 6 (B/T), 11 x 10 x 4 (B/T)	Pancreatic LN	Dissemination (adrenal glands), LNs (mesenteric)
10	1177	60	F	12.8	*KPPC*	Mirogabalin	PDAC, moderately to poorly/sarcomatoid + focal anaplastic carcinoma	717.1	18 x 6 x 5 (H/B/T), 10 x 4 x 4 (H/B)	Duodenum	No

* ND, Not determined due to dead found mouse; ** PDAC, Pancreatic ductal adenocarcinoma; ***, Pancreatic head (H), body (B), tail (T)

No.	ID #	Age (days)	Sex	Body weight (g)	Mouse	Administration	Histological phenotype	Pancreatic weight (mg)	Tumour size (mm) and Location	Direct invasion	Metastasis/Dissemination
1	339	70	M	22.5	Normal	Vehicle	Normal pancreas	667.9	No tumour		
2	352	70	M	25.0	Normal	Vehicle	Normal pancreas	486.3	No tumour		
3	353	70	M	27.6	Normal	Vehicle	Normal pancreas	366.6	No tumour		
4	331	80	M	25.5	Normal	Vehicle	Normal pancreas	470.4	No tumour		
5	333	80	M	24.5	Normal	Vehicle	Normal pancreas	491.2	No tumour		
6	439	80	M	21.5	Normal	Vehicle	Normal pancreas	326.0	No tumour		
7	328	80	F	20.9	Normal	Vehicle	Normal pancreas	484.6	No tumour		
8	336	80	F	19.6	Normal	Vehicle	Normal pancreas	349.5	No tumour		
9	330	80	F	21.3	Normal	Vehicle	Normal pancreas	370.6	No tumour		
10	368	120	M	22.1	Normal	Vehicle	Normal pancreas	384.9	No tumour		
11	374	120	F	17.3	Normal	Vehicle	Normal pancreas	521.4	No tumour		
12	327	160	M	25.0	Normal	Vehicle	Normal pancreas	427.6	No tumour		
1	1097	75	M	29.3	Normal	Mirogabalin	Normal pancreas	698.5	No tumour		
2	1100	75	M	29.3	Normal	Mirogabalin	Normal pancreas	564.5	No tumour		
3	1104	76	M	23.5	Normal	Mirogabalin	Normal pancreas	506.3	No tumour		
4	1105	76	M	23.8	Normal	Mirogabalin	Normal pancreas	474.6	No tumour		
5	1133	74	F	18.5	Normal	Mirogabalin	Normal pancreas	348.9	No tumour		
6	1134	74	F	19.3	Normal	Mirogabalin	Normal pancreas	399.7	No tumour		
7	1152	74	F	18	Normal	Mirogabalin	Normal pancreas	508	No tumour		
8	1164	70	F	22.5	Normal	Mirogabalin	Normal pancreas	483.4	No tumour		

Supplementary Table 4. Direct invasion of PDAC to other tissue/organ

Administration	Positive (%)	Negative (%)	*P**
Vehicle	11 (78.6)	3 (21.4)	1.000
Mirogabalin	8 (80.0)	2 (20.0)	

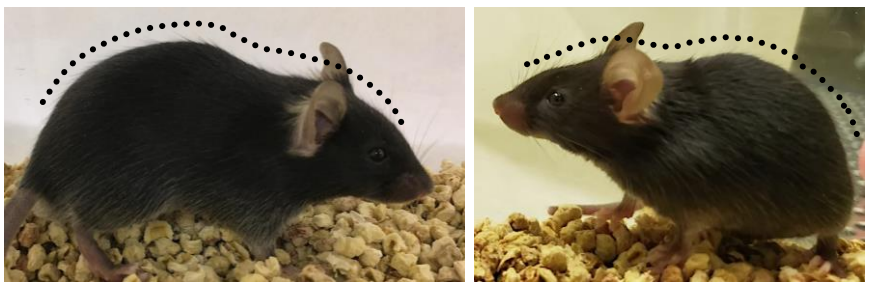
* analysed by Chi-squared test

Supplementary Table 5. Distant metastasis/dissemination of PDAC

Administration	Positive	Negative	*P**
Vehicle	7 (50.0)	7 (50.0)	0.9448
Mirogabalin	6 (60.0)	4 (40.0)	

* analysed by Chi-squared test

A



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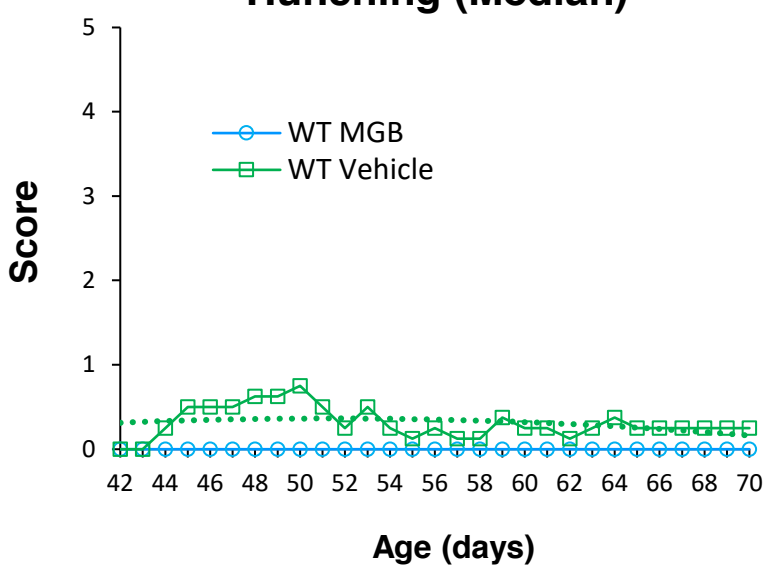

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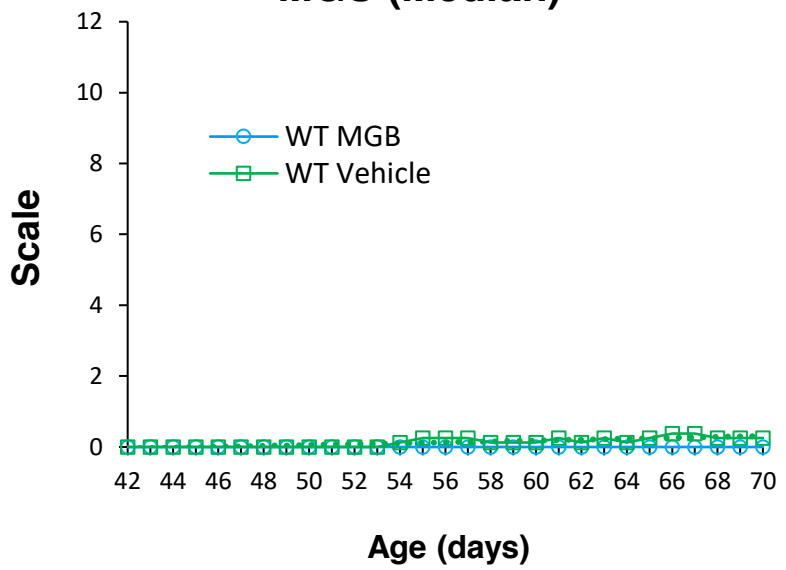

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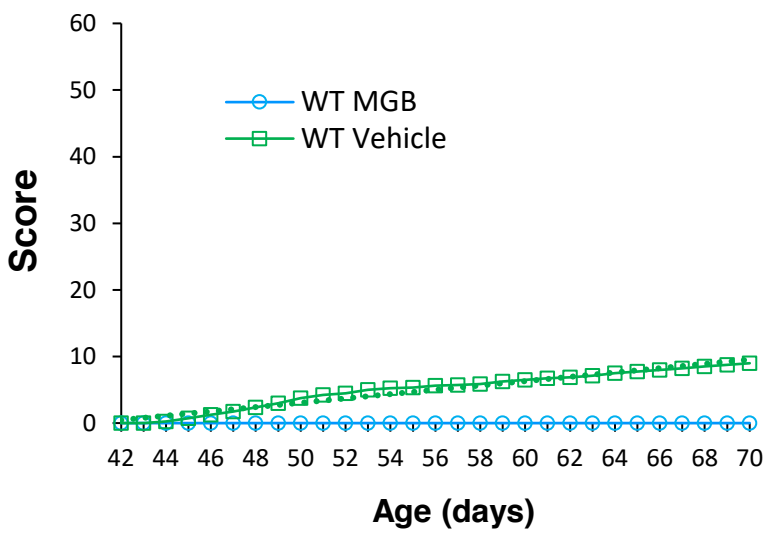

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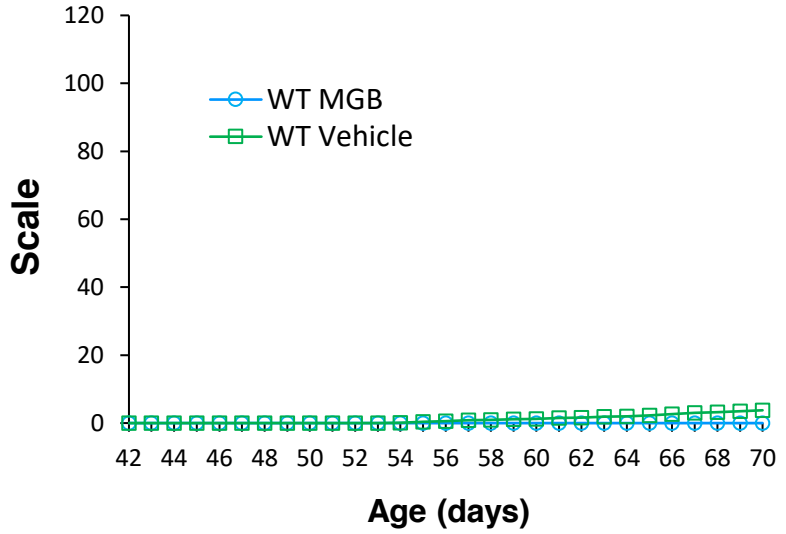
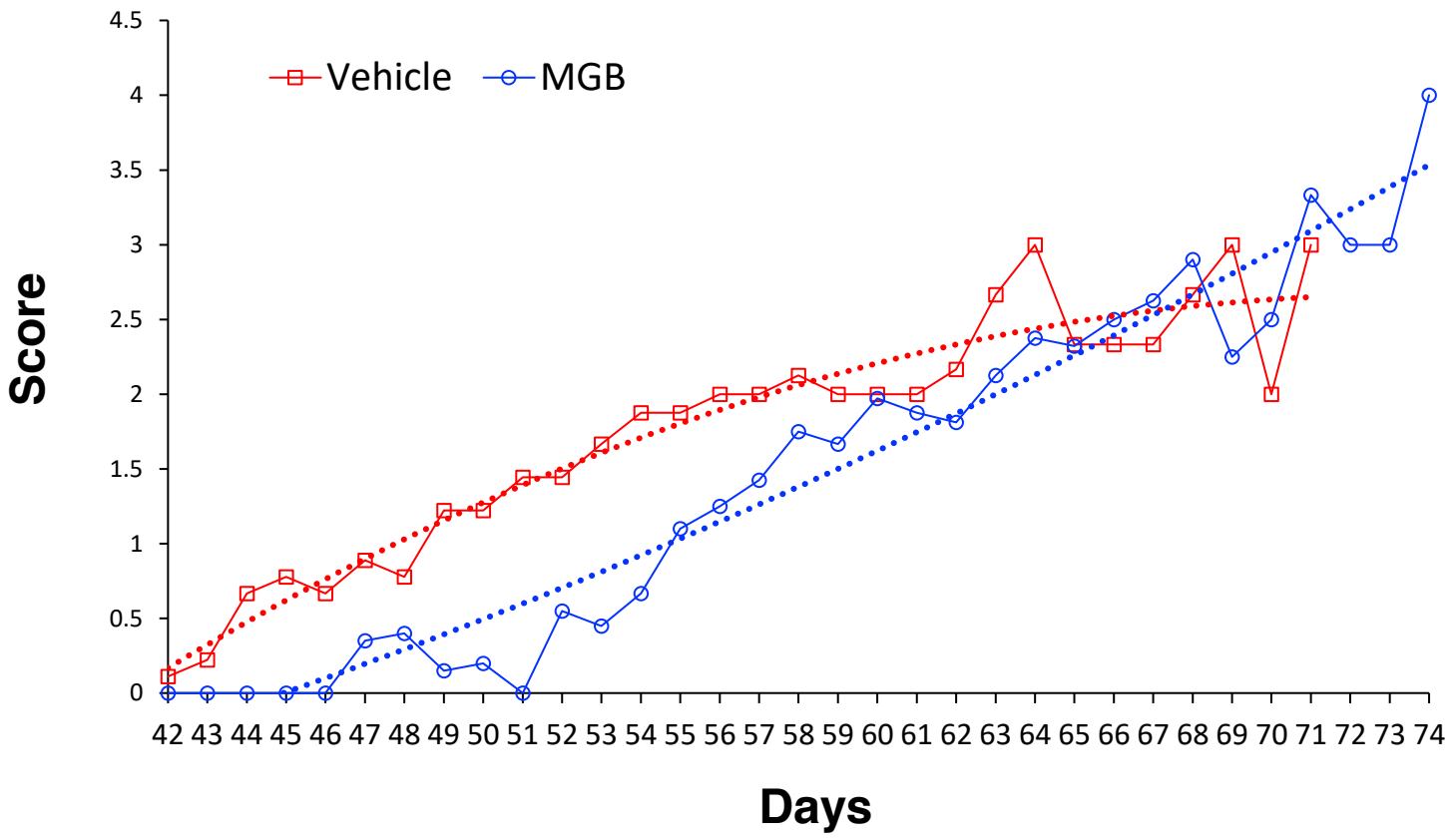


Supplementary Figure 1. Itaya T, et al.

A



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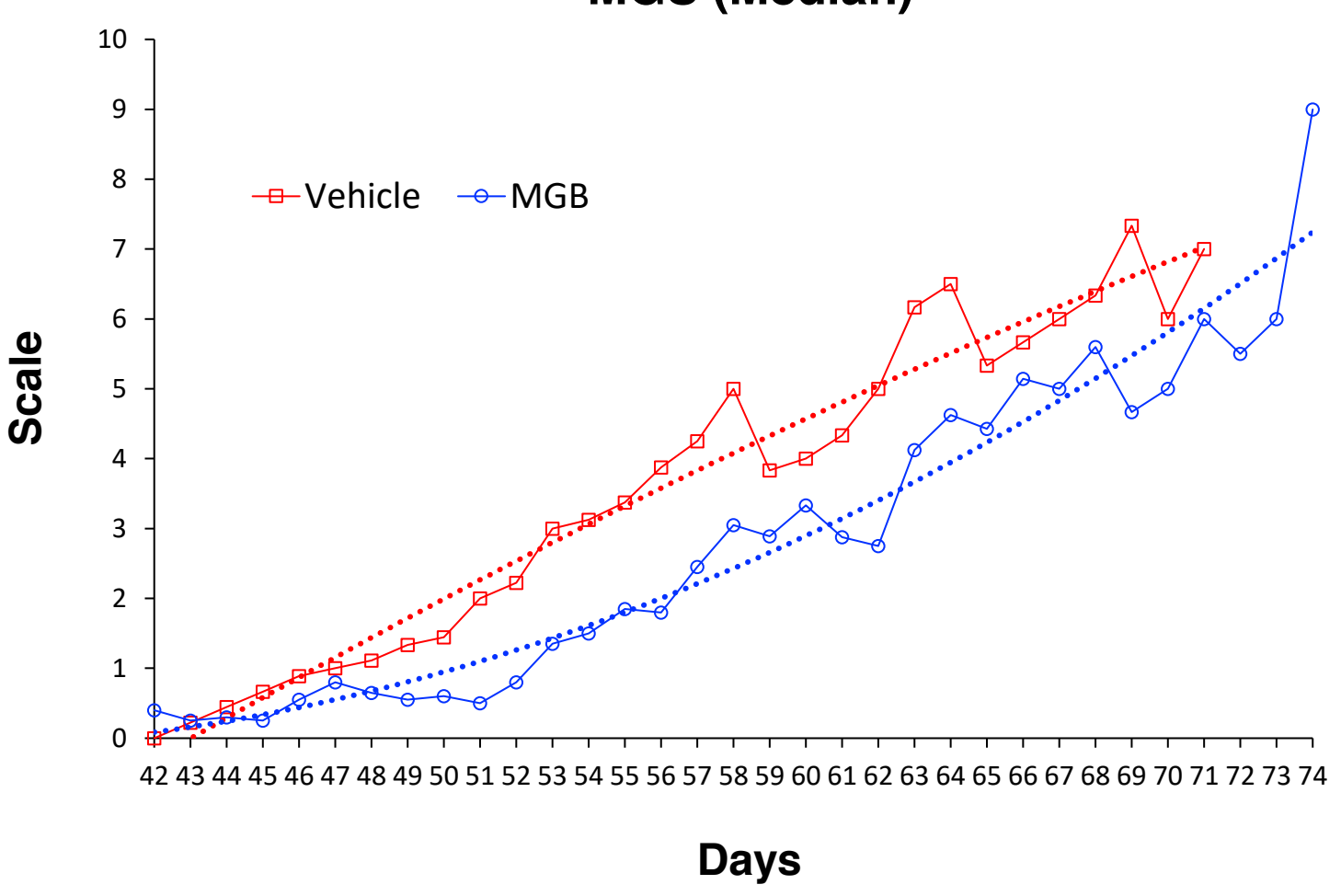
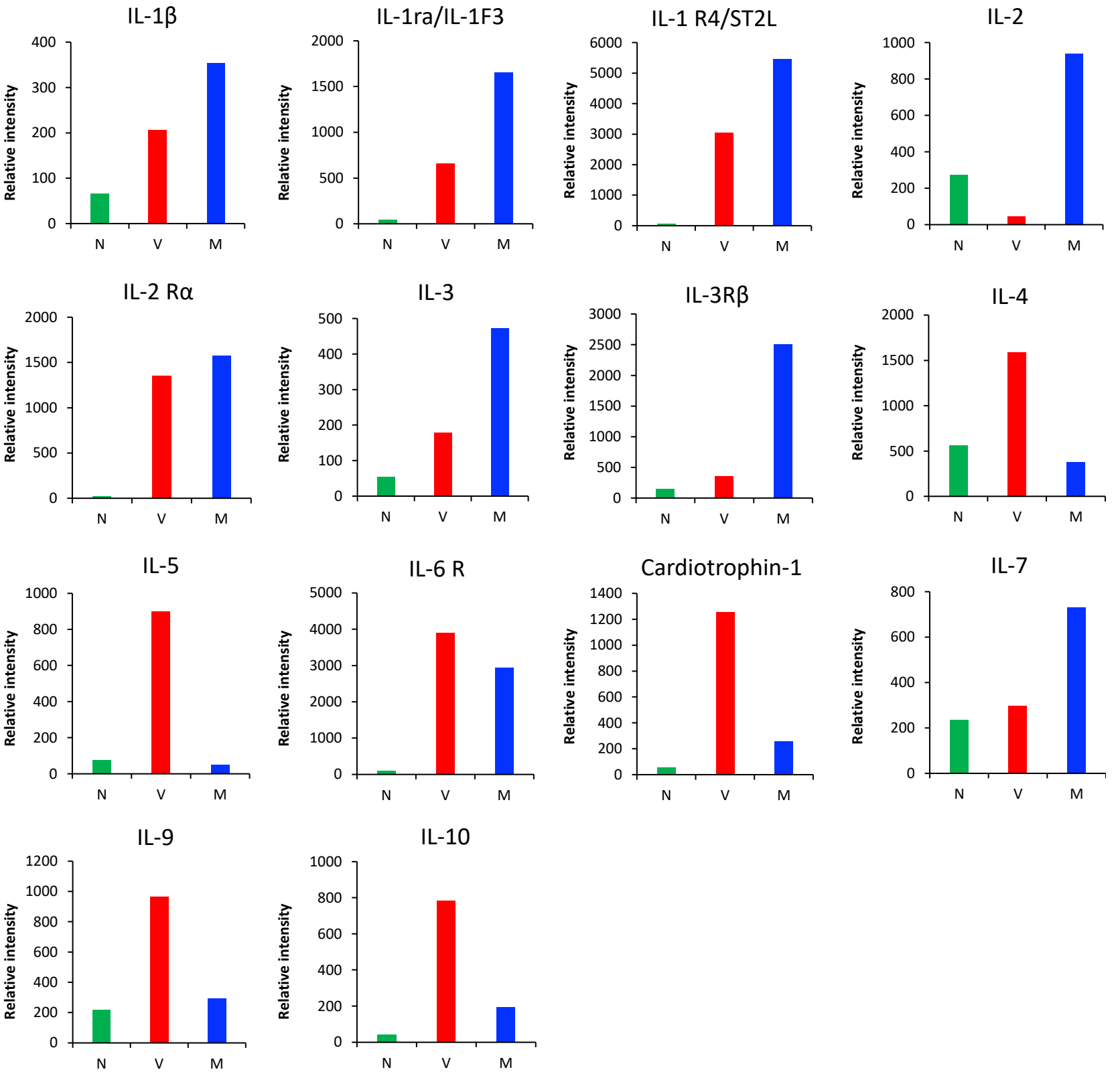


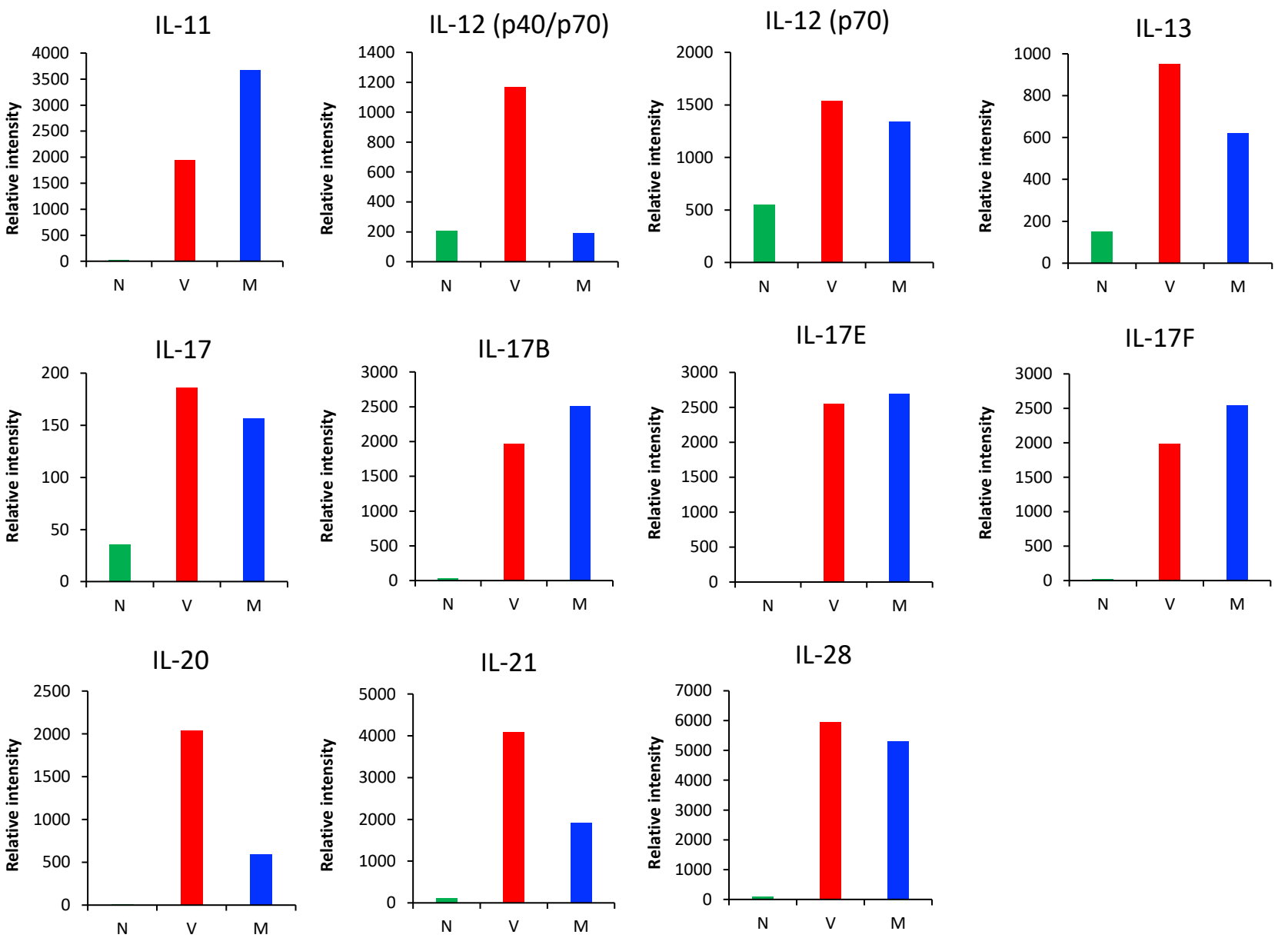
Supplementary Figure 2. Itaya T, et al.

Interleukins (ILs) and the related molecules (1)



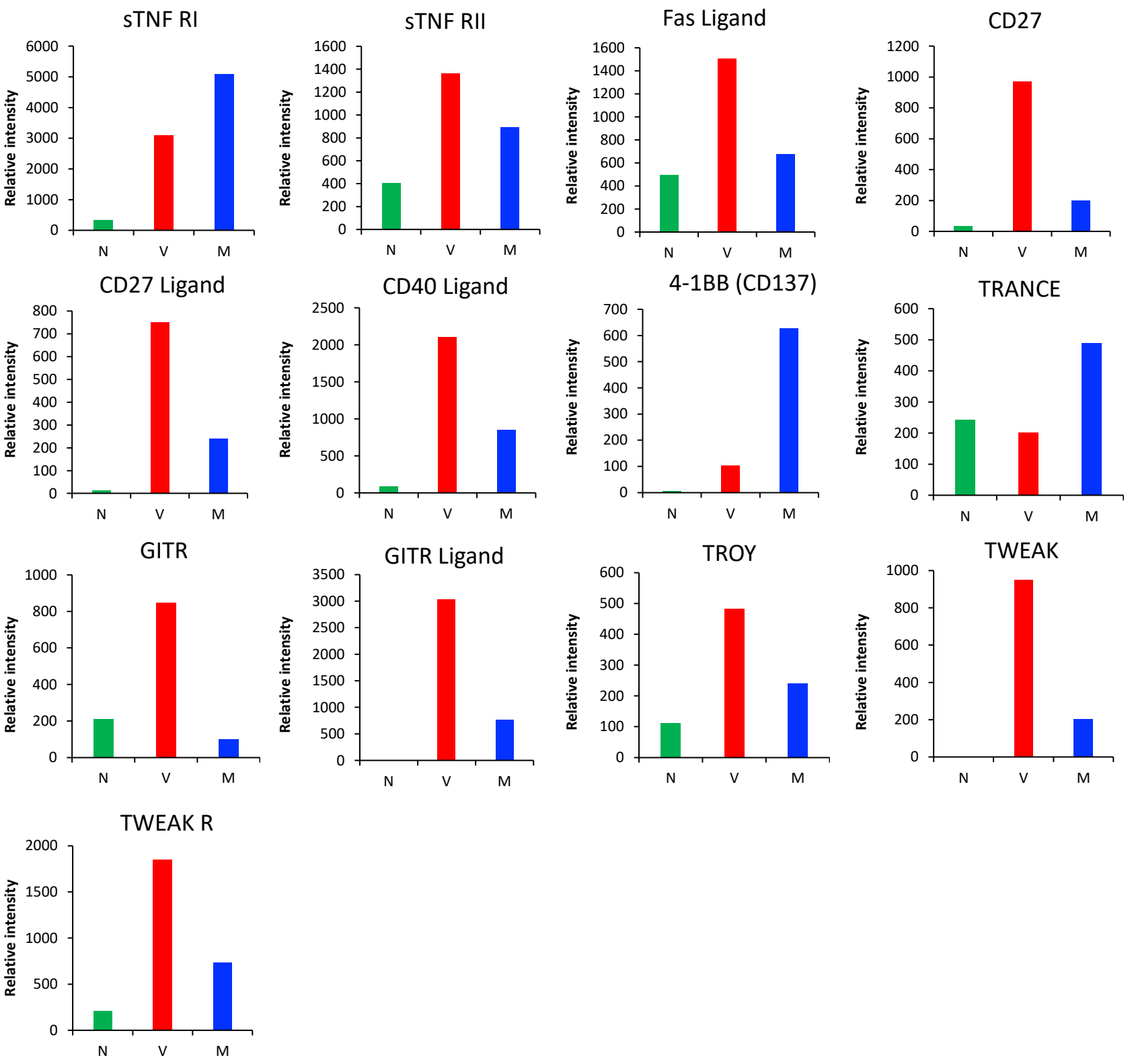
Supplementary Figure 3. Itaya T, et al.

Interleukins (ILs) and the related molecules (2)



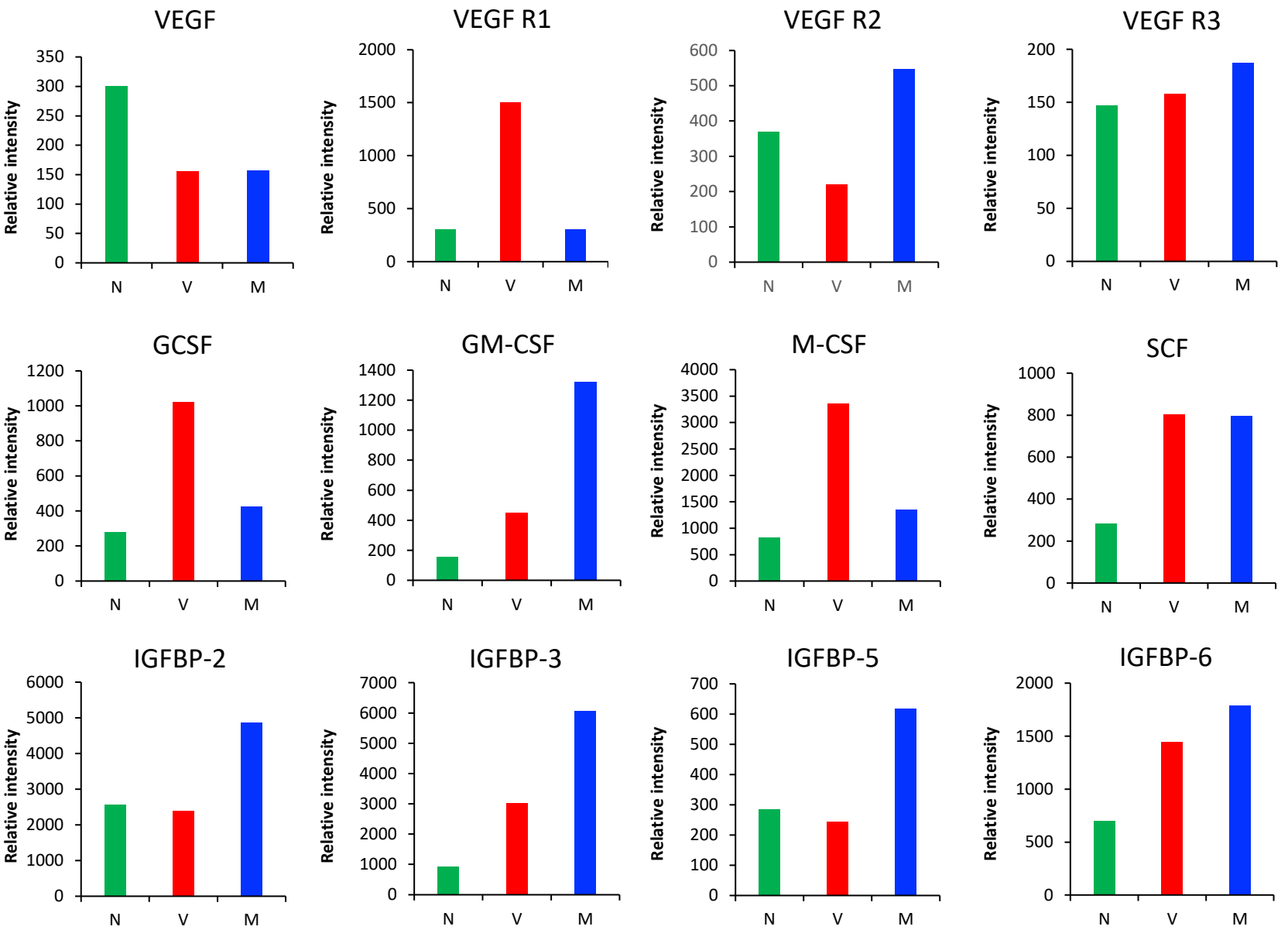
Supplementary Figure 4. Itaya T, et al.

TNF-related molecules

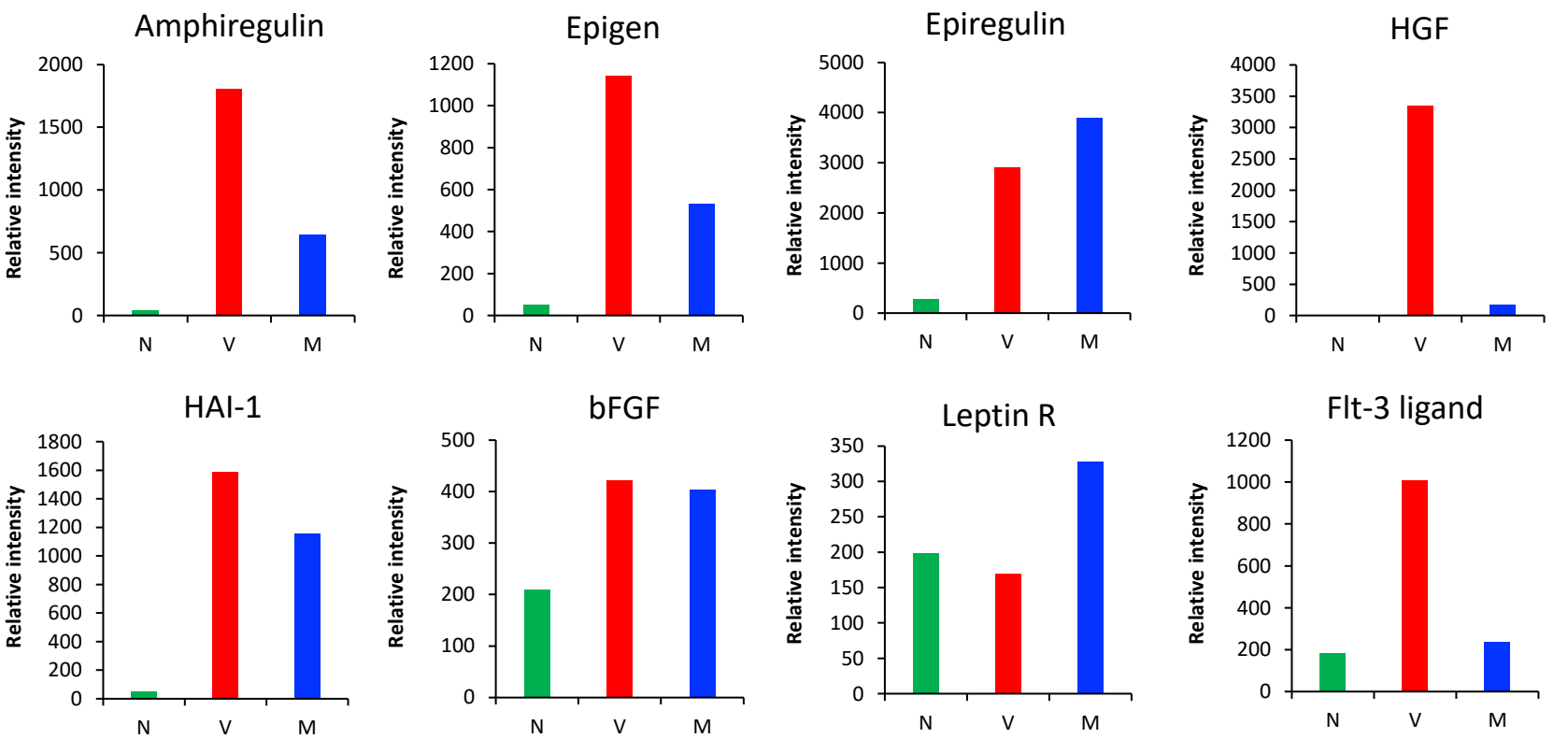


Supplementary Figure 5. Itaya T, et al.

Growth factor and the related molecules (1)

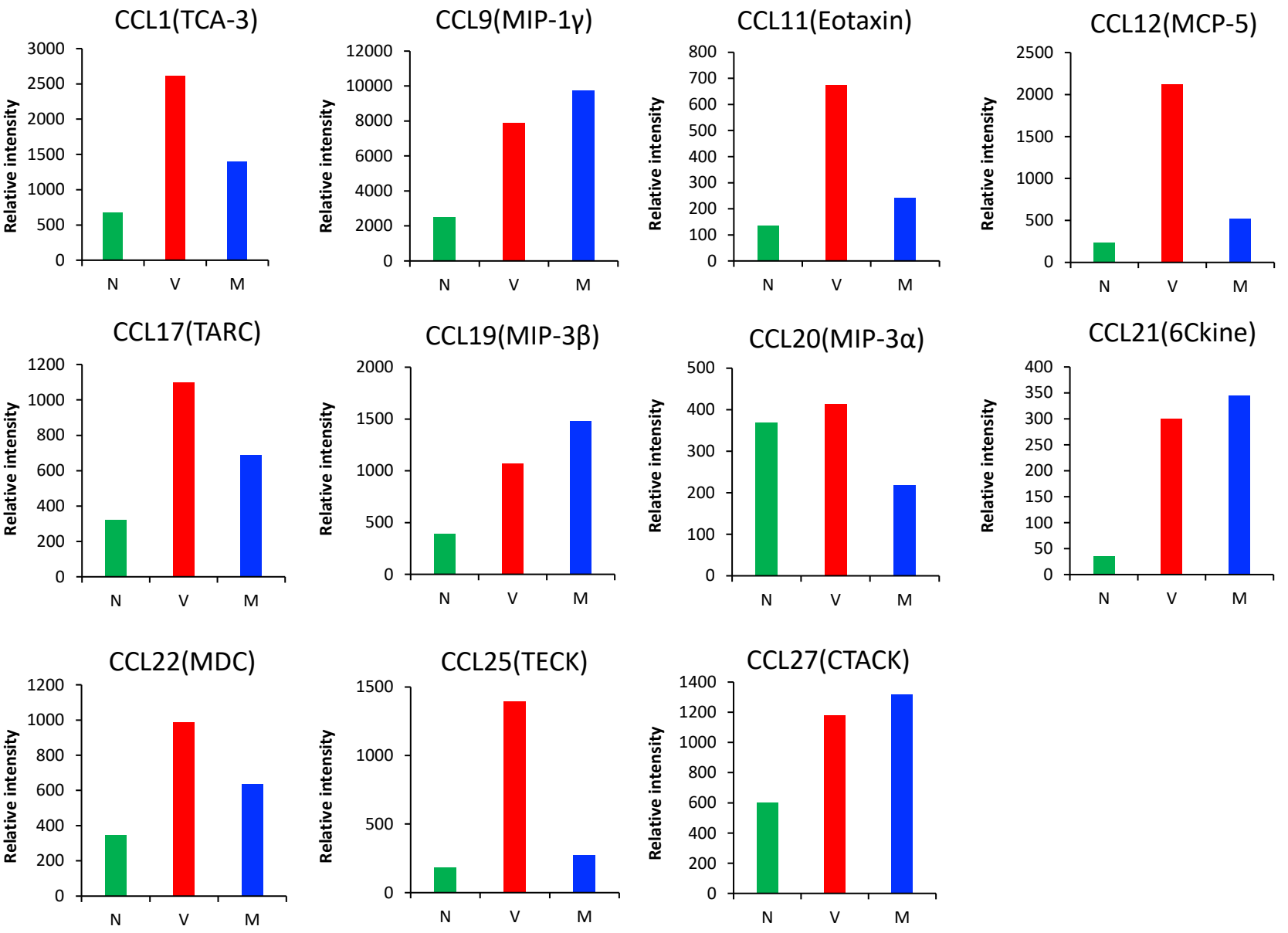


Growth factor and the related molecules (2)

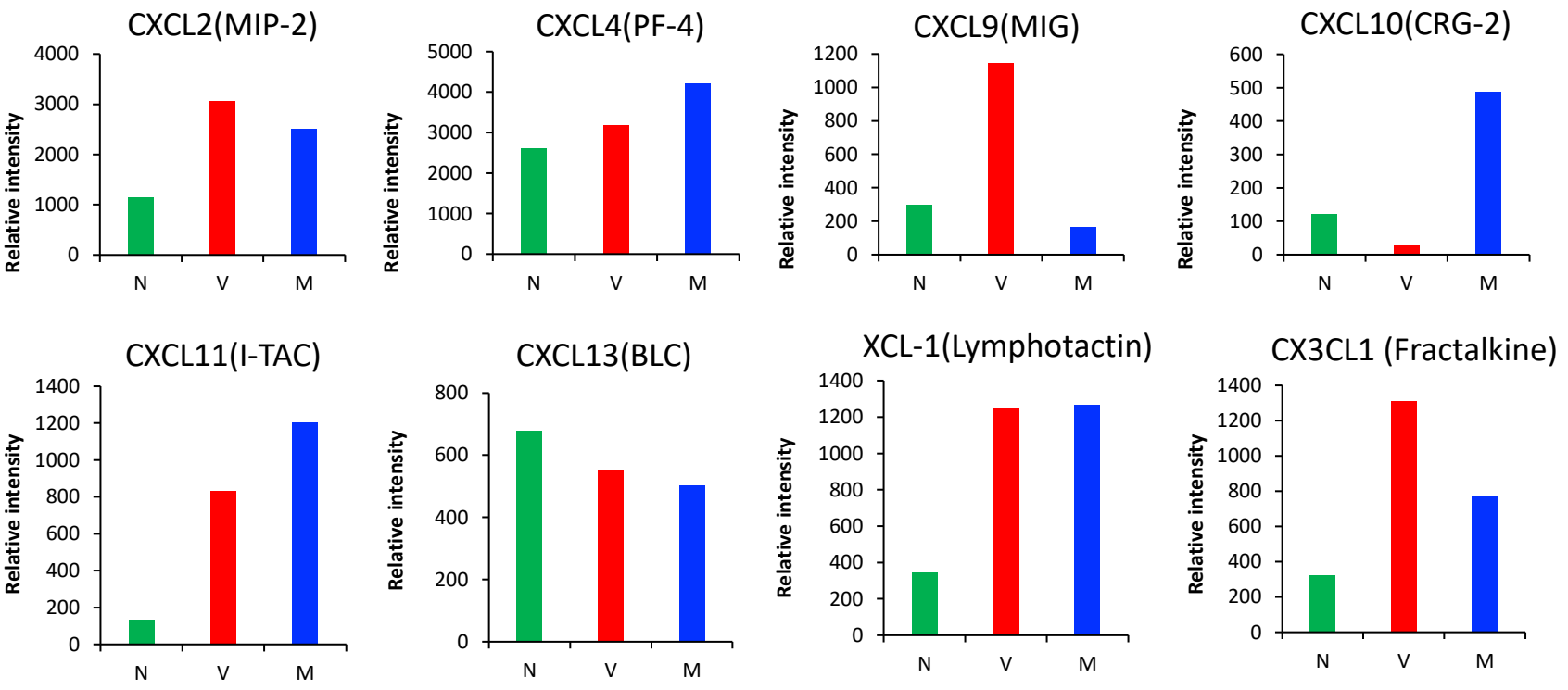


Supplementary Figure 6. Itaya T, et al.

Other CCLs

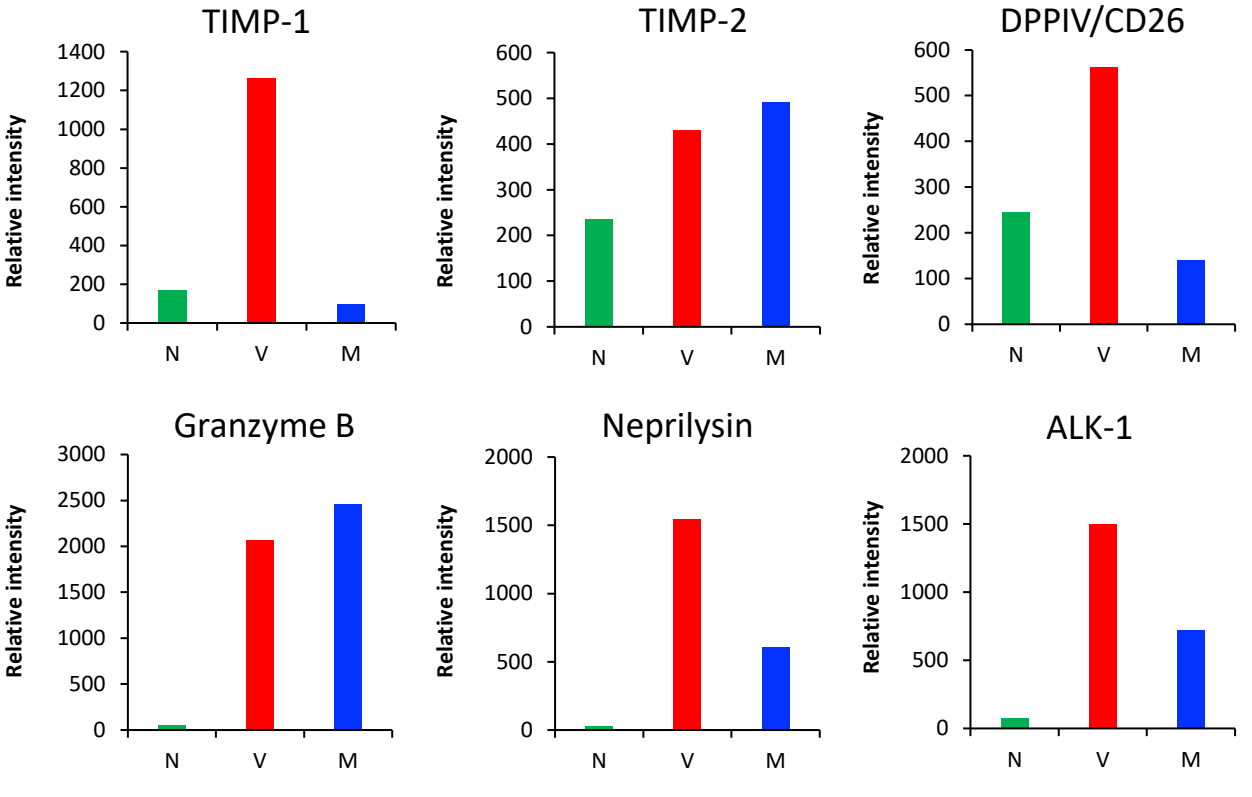


Other CXCLs, XCL-1, and CX3CL1

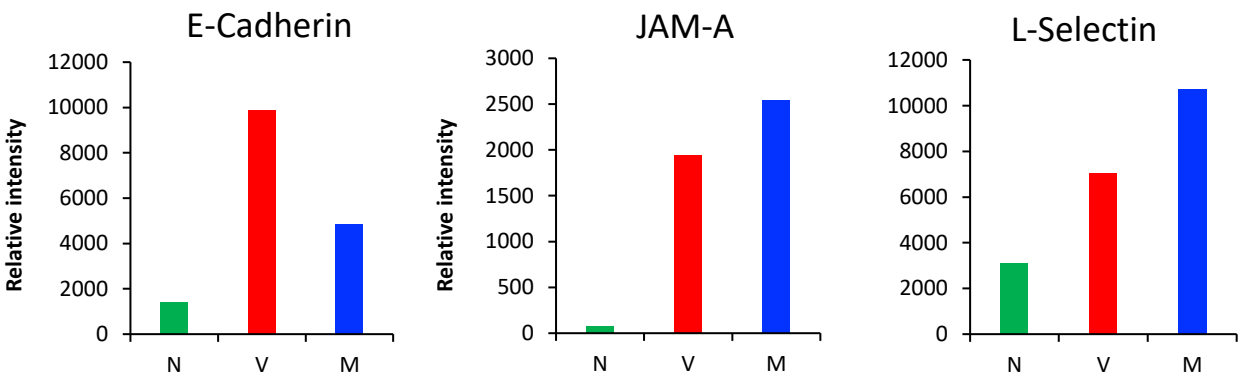


Supplementary Figure 7. Itaya T, et al.

TIMPs and other proteases

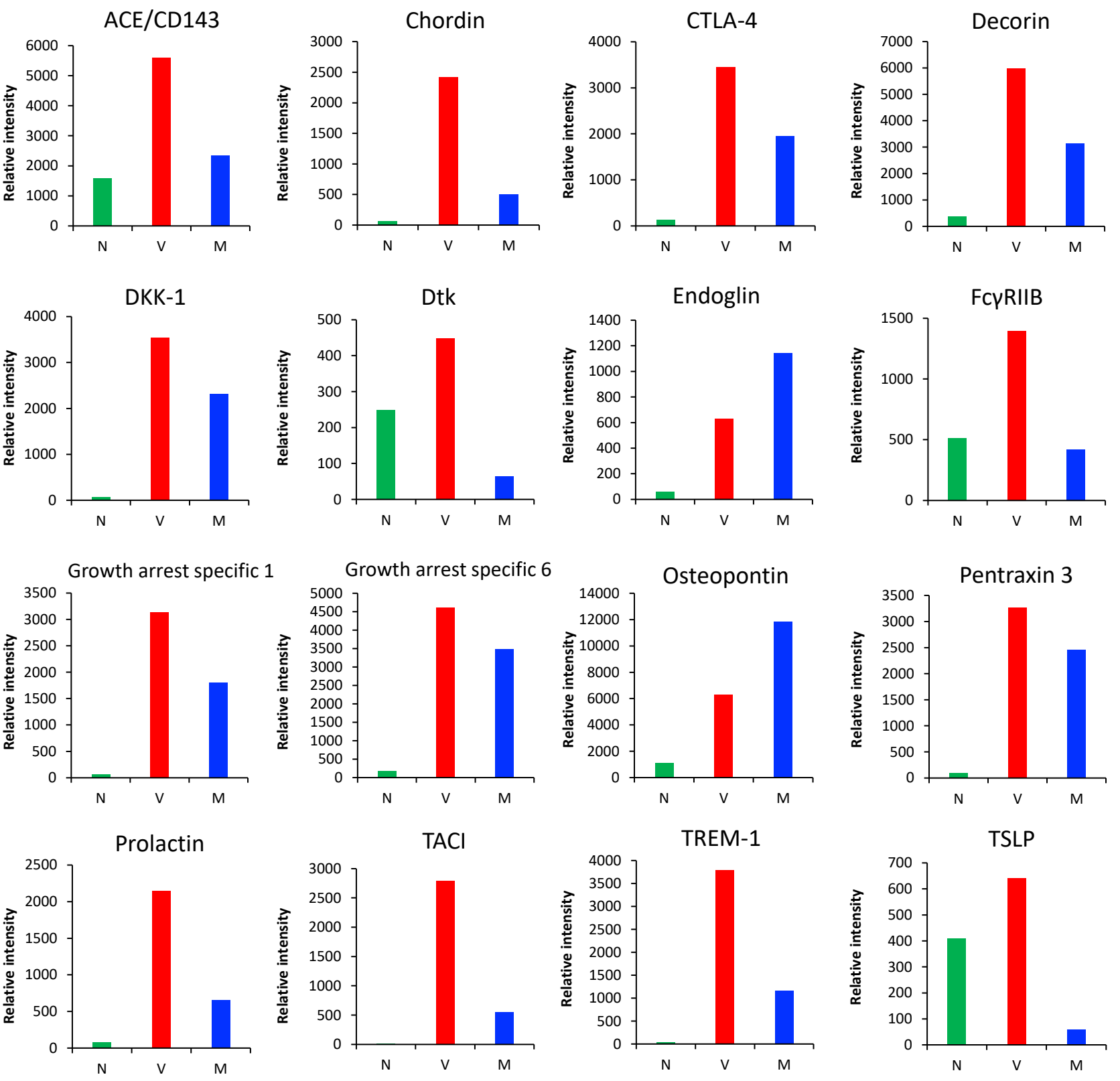


Adhesion Molecules



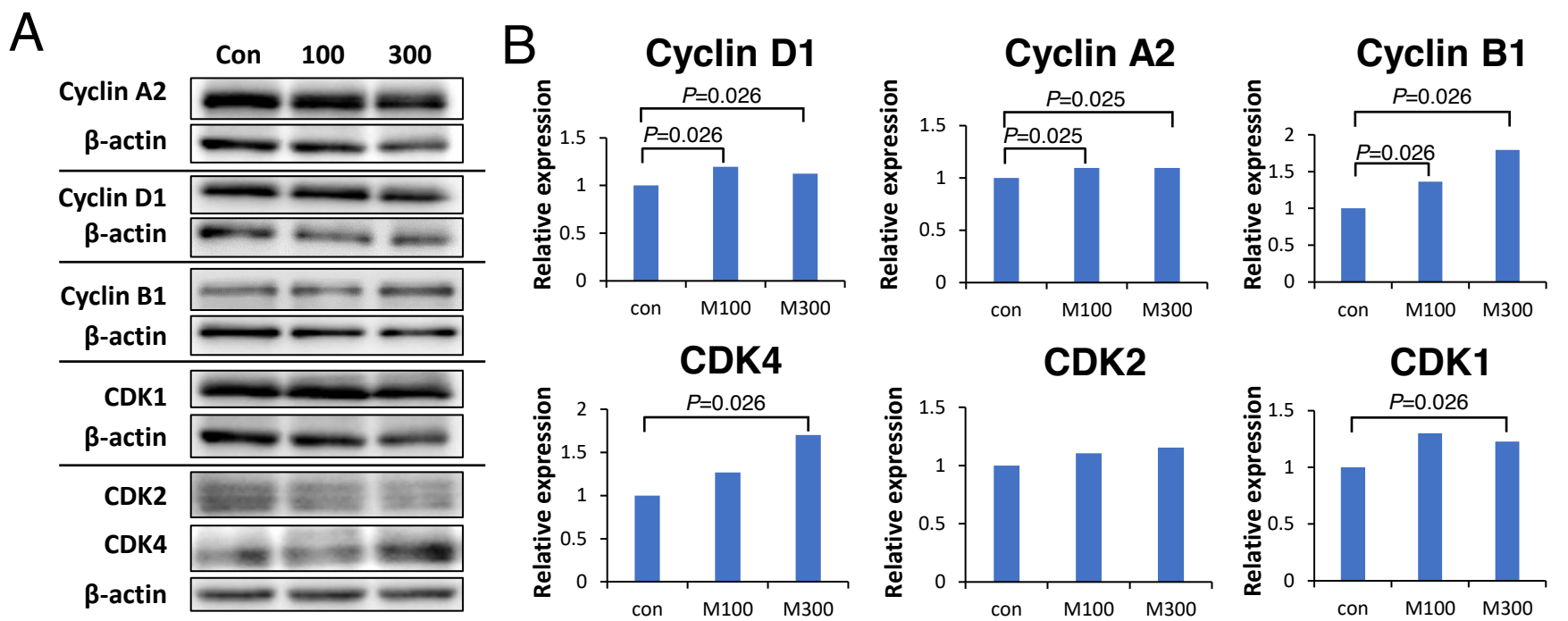
Supplementary Figure 8. Itaya T, et al.

Other molecules

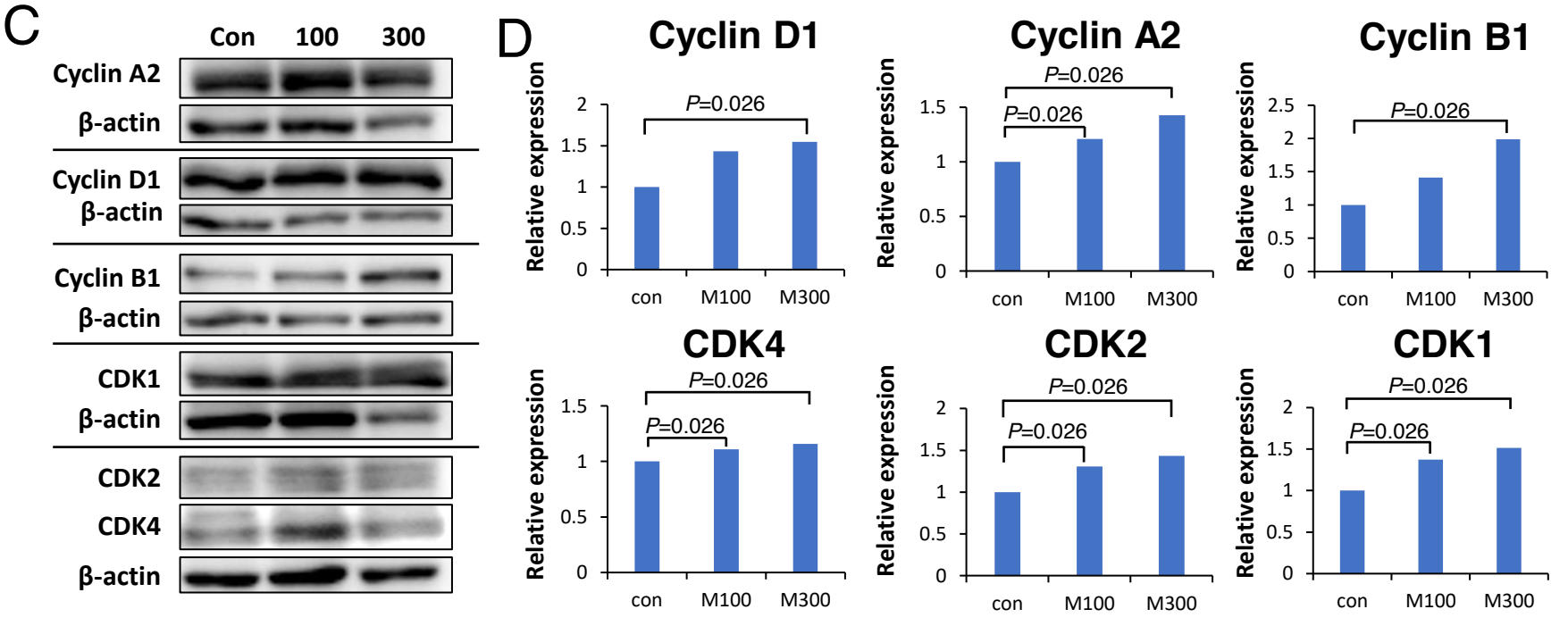


Supplementary Figure 9. Itaya T, et al.

PDAC cell line (#147)



PDAC cell line (#244)



Supplementary Figure 10. Itaya T, et al.

Supplementary Figure 1. Healthy mouse with the administration of MGB and vehicle water (A). Median hunching score (B) and MGS (C) and cumulative hunching score (D) and MGS (E). MGB, mirogabalin; MGS, mouse grimace scale; WT, healthy mouse with normal pancreas.

Supplementary Figure 2. Hunching score (A) and MGS (B) in *KPPC* mice treated with/without MGB. Data are presented as median. MGB, mirogabalin; MGS, mouse grimace scale.

Supplementary Figures 3–9. Cytokine antibody array showing the pooled plasma levels of cytokines in healthy control mice (N; n = 4) and *KPPC* mice treated with MGB (M; n = 6), or *KPPC* mice treated with vehicle water (V; n = 4). Data are presented as the medians of four array spots. ACE, angiotensin-converting enzyme; Alk-1, anaplastic lymphoma kinase-1; bFGF, basic fibroblast growth factor; CCL, CC chemokine ligand; CTLA-4, cytolytic T lymphocyte-associated antigen 4; CXCL, C-X-C motif ligand; DKK-1, dickkopf-1; DPPIV, dipeptidyl peptidase-4; GAS, growth arrest specific; GCSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte–macrophage colony-stimulating factor; GITR, glucocorticoid-induced tumor necrosis factor receptor; HGF, hepatocyte growth factor; IGFBP, insulin-like growth factor binding protein; IL, interleukin; JAM-A, junctional adhesion molecule-A; MAdCAM-1, mucosal addressing cell adhesion molecule 1; M-CSF, macrophage colony-stimulating factor; MMP, matrix metalloproteinases; SCF, stem cell factor; TIMP, tissue inhibitors of metalloproteinases; TNF, tumor necrosis factor; TPO, thrombopoietin; TRANCE, TNF-related activation-induced cytokine; TREM-1, triggering receptor expressed on myeloid cells 1; TSLP, thymic stromal lymphopoietin;

TWEAK, tumor necrosis factor-like weak inducer of apoptosis; VEGF, vascular endothelial growth factor.

Supplementary Figure 10. Immunoblotting of cyclins D1, A2, B1, CDK4, CDK2, and CDK1 in mouse PDAC cells (#147, 244) (A). Quantification of the data in a (B) (Con, control; M100, 100-μM MGB; M300, 300-μM MGB). Significance was determined by non-parametric Steel's multiple comparison test. CDK, cyclin-dependent kinase; PDAC, pancreatic ductal adenocarcinoma.